

The diagram illustrates a bispecific antibody molecule. It features two Fab arms, each composed of heavy chain (H) and light chain (L) domains. The variable regions (VH and VL) are shown at the tips of the arms, while the constant regions (CH1 and CL) form the base. The arms are connected by a hinge region (S) and a stem region (CH2, CH3). Labels include dAb, H, Fab, L, VH, VL, CH1, CL, S, CH2, CH3, Fd, Fv, and ABS.



Fig.2a

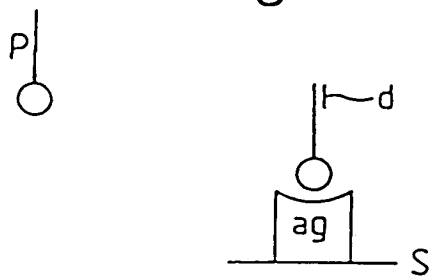


Fig.2b

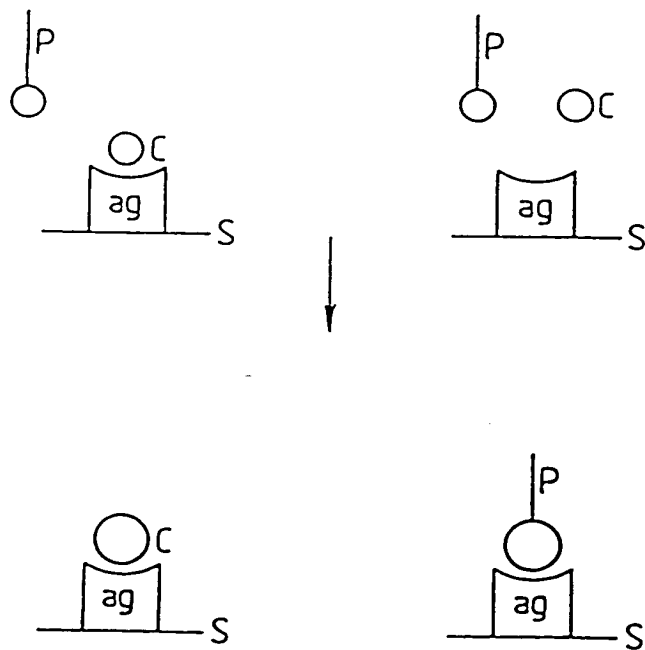
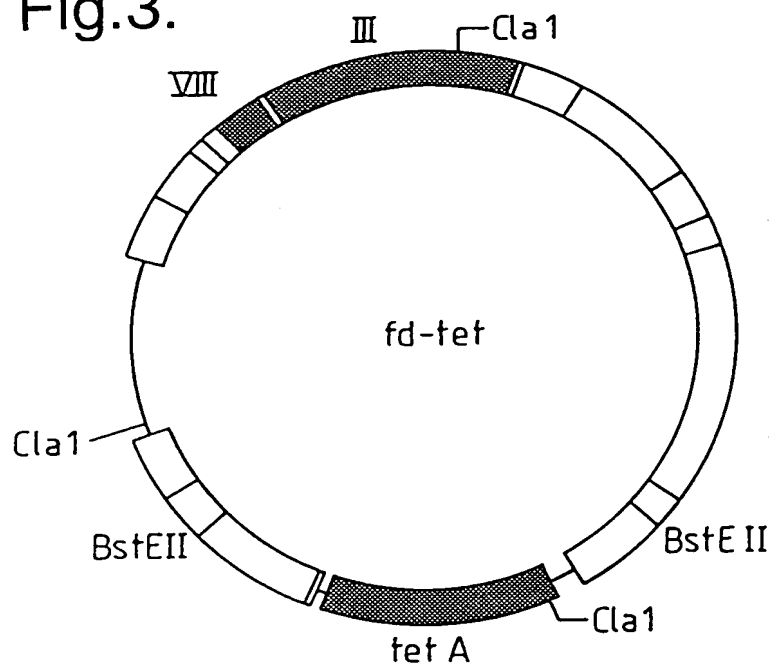


Fig.3.



fd - tet
 ~
 cleave with BstEII
 ~
 fill in with Klenow
 ~
 re-ligate
 ↓
 FDT6Bst
 ~
 in vitro mutagenesis (oligo 1)
 ↓
 FDTPs/Bs
 ~
 in vitro mutagenesis (oligo 2)
 ↓
 FDTPs/Xh

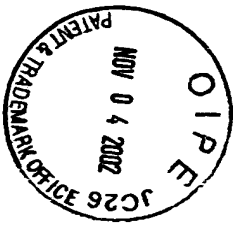


Fig.4 a

Oligo 1 (1653) ACA ACT TTC AAC AGT TGA GGA GAC GGT GAC CGT AAG CTT CTG CAG TTG GAC CTG AGC (SEQ ID NO. 177)
GGA GTG AGA ATA (1620)
Oligo 2 (1653) ACA ACT TTC AAC AGT TTC CCG TTT GAT CTC GAG CTC CTG CAG TTG GAC CTG (SEQ ID NO. 178)
(1704)
Oligo 3 GTC GTC TTT CCA GAC GTT AGT (SEQ ID NO. 179)

Fig.4 b

GENE III
SIGNAL
CLEAVAGE SITE
(1624)
A TCT CAC TCC GCT
(1650)
GAA ACT GTT GAA AGT (SEQ ID NO. 180)
Q V Q L Q (SEQ ID NO. 1) V T V S S (SEQ ID NO. 2)
B TCT CAC TCC GCT CAG GTC CAA CTG CAG AAG CTT ACG GTC ACC GTC TCC TCA ACT GTT GAA AGT (SEQ ID NO. 181)
PstI
BstEII
Q V Q L Q (SEQ ID NO. 1) L E I K R (SEQ ID NO. 3)
C TCT CAC TCC GCT CAG GTC CAA CTG CAG GAG CTC GAG ATC AAACGG GAA ACT GTT GAA AGT (SEQ ID NO. 182)
PstI
XhoI

Fig.5a



Fig.5 b

E T V T I T C R A S G N I H N Y L A W Y
GAAACTGTCACCATCACATGTCGAGCAAGTGGGAATATTCACAATTATTTAGCATGGTAT
550 560 570 580 590 600

Q Q K Q G K S P Q L L V Y Y T T T L A D
CAGCAGAAACAGGGAAAATCTCCTCAGCTCCTGGTCTATTATACAACAACCTTAGCAGAT
610 620 630 640 650 660

VKD1.3

G V P S R F S G S G S G T Q Y S L K I N
GGTGTGCCATCAAGGTTTCAGTGGCAGTGGATCAGGAACACAATATTCTCTCAAGATCAAC
670 680 690 700 710 720

S L Q P E D F G S Y Y C Q H F W S T P R
AGCCTGCAACCTGAAGATTTTGGGAGTTATTACTGTCAACATTTTGGAGTACTCCTCGG
730 740 750 760 770 780

Myc Tag (TAG1)

T F G G G T K L E I K R E O K L I S E E
ACGTTCCGGTGGAGGGACCAAGCTCGAGATCAAACGGGAACAAAACTCATCTCAGAAGAG
790 800 810 820 830 840

XhoI

D L N * * (SEQ ID NO. 183)

GATCTGAATTAATAATGATCAAACGGTAATAAGGATCCAGCTCGAATTC (SEQ ID NO. 184)
850 860 870 880

EcoRI

Fig.6.

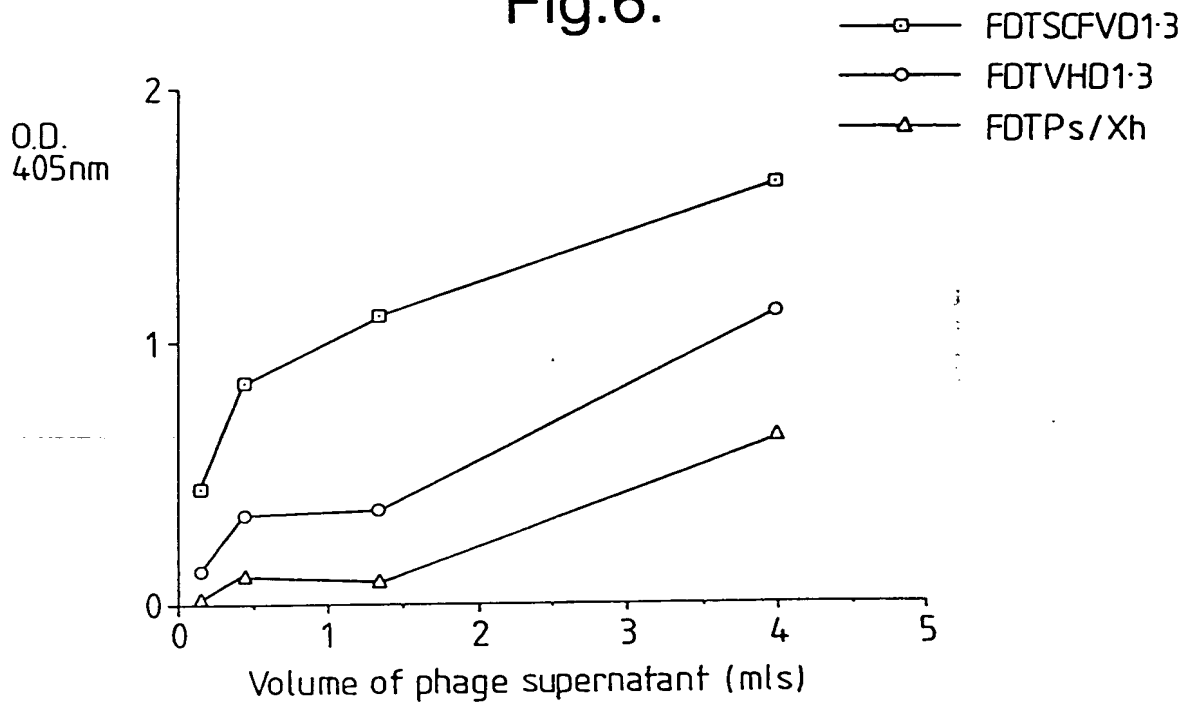


Fig.7.

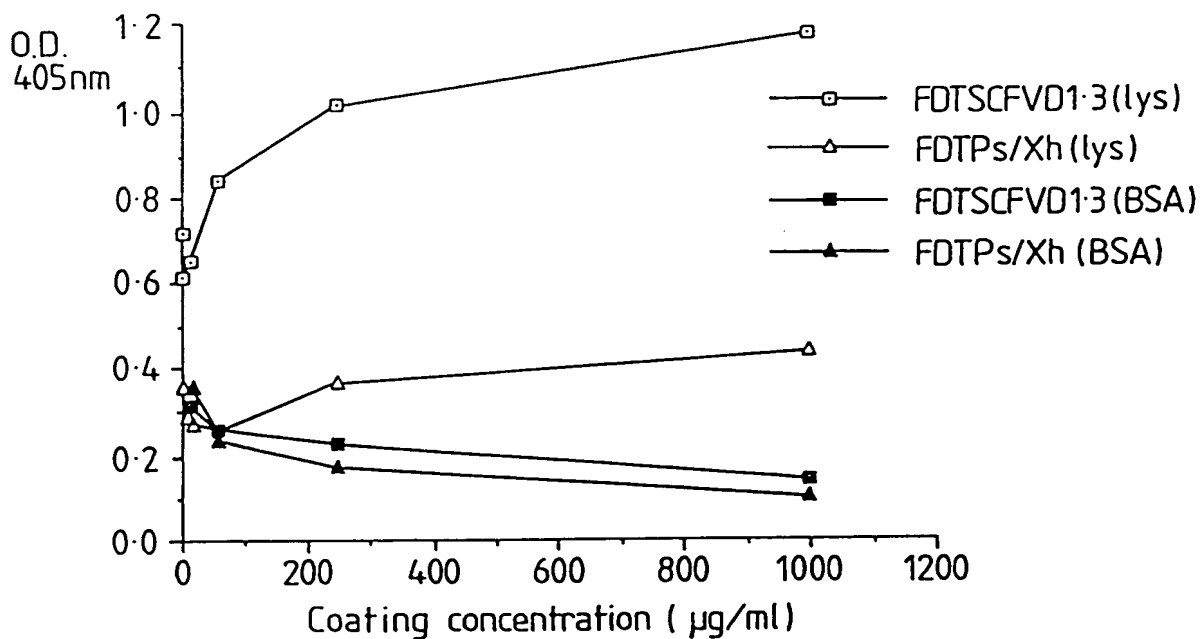




Fig.10a

M K Y L L P T A A
GCATGCCAAATTCTATTTC AAGGAGACAGTCATAATGAAATACCTATTGGCTACGGCAGCC
10 20 30 40 50 60

A G L L L L A A Q P A M A Q V Q L Q E S
GCTGGATTGTTATTACTGCTGCCCCAACCAGCGATGGCCCTGGTGCAGCTGCAGGAGTCA
70 80 90 100 110 120

G P G L V A P S Q S L S I T C T V S G F
GGACCTGGCCTGGTGGCGCCCTCAGAGAGCCTGTCCATCACATGCACCGTCTCAGGGTTC
130 140 150 160 170 180

S L T G Y G V N W V R Q P P G K G L E W
TCATTAAACGGCTATGGTGTAAACTGGGTTCCGCCAGCCTCCAGGAAAGGGTCTGGAGTGG
190 200 210 220 230 240

L G M I W G D G N T D Y N S A L K S R L
CTGGGAATGATTTGGGGTGATGGAAACACAGACTATAATTACAGCTCTCAAATCCAGACTG
250 260 270 280 290 300

S I S K D N S K S Q V F L K M N S L H T
AGCATCAGCAAGGACAACCTCCAAGAGCCAAGTTTTCTTAAAAATGAACAGTCTGCACACT
310 320 330 340 350 360

D D T A R Y Y C A R E R D Y R L D Y W G
GATGACACAGCCAGGTACTACTGTGCCAGAGAGAGAGATTATAGGCTTGACTACTGGGGC
370 380 390 400 410 420

Q G T T V T V S S A S T K G P S V F P L
CAAGGCACCAACGGTCAACGTCTCTCTCAGCCTCCACCAAGGGCCCATCGGTCTTCCCCCTG
430 440 450 460 470 480

A P S S K S T S G G T A A L G C L V K D
GCACCCCTCCTCCAAGAGCACCTCTGSGGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGAC
490 500 510 520 530 540



Fig.10b

Y F P E P V T V S W N S G A L T S G V H
TACTTCCCCGAACCGGTGACGGTGTCTGTGGAACCTCAGGCGCCCTGACCAGCGCGGTGCAC
550 560 570 580 590 600

T F P A V L Q S S G L Y S L S S V V T V
ACCTTCCCGGCTGTCTACAGTCTCTAGCACTCTACTCCCTCAGCAGCGGTGTGACCGTG
610 620 630 640 650 660

P S S S L G T Q T Y I C N V N H K P S N
CCCTCCAGCAGCTTGGGCAACCCAGACCTACATCTGCAACGTGAATCACAAGCCCCAGCAAC
670 680 690 700 710 720

T K V D K K V E P K S S * * (SEQ ID NO. 187)
ACCAAGGTGACACAAGAAAGTTCGCCCCAAATCTTCATAATAACCCGGGAGCTTGCATGCA
730 740 750 760 770 780

M K Y L L P T A A A G L
AATTCATTTTCAAGGACACAGTTCATTAATGAATACTTATTCCTAAGGCAGCCGCTGGAT
790 800 810 820 830 840

L L L A A Q P A M A D I E L T Q S P A S
TGTTATTAAGTCTGCTGCCCCAACCAAGCATGGCCGACATCGAGCTCACCAGTCTCCAGCCT
850 860 870 880 890 900

L S A S V G E T V T I T C R A S G N I H
CCCTTTCTGCGTCTGTGGGAGAACTGTACCATCACATGTGAGCAAGTGGGAATATTC
910 920 930 940 950 960

N Y L A W Y Q Q K Q G K S P Q L L V Y Y
ACAATTATTAGCATGGTATCAGCAGAAACAGGGAAAATCTCTCAGCTCCTGGTCTATT
970 980 990 1000 1010 1020



Fig.10 c

T T T L A D G V P S R F S G S G S G T Q
ATACAACAACCTTAGCAGATGGTGTGCCATCAAGGTTTCAGTGGCAGTGGATCAGGAACAC
1030 1040 1050 1060 1070 1080

Y S L K I N S L Q P E D F G S Y Y C Q H
AATATTCTCTCAAGATCAACAGCCTGCGCCTGAAGATTTTGGGAGTTATTACTGTCAAC
1090 1100 1110 1120 1130 1140

F W S T P R T F G G G T K L E I K R T V
ATTTTGGGAGTACTCTCGGACGTTGGTGGAGGCCACCAAGCTCGAGATCAAAACGGACTG
1150 1160 1170 1180 1190 1200

A A P S V F I F P P S D E Q L K S G T A
TGGCTGCACCATCTGTCTTCATCTTCCCGCCATCTGATGAGCAGTTGAAATCTGGAAGT
1210 1220 1230 1240 1250 1260

S V V C L L N N F Y P R E A K V Q W K V
CCTCTGTGTGTGCTGCTGAATAACTTCTATCCCGAGAGGCCAAAGTACAGTGGGAAGG
1270 1280 1290 1300 1310 1320

D N A L Q S G N S Q E S V T E Q D S K D
TGGATAACGCCCTCCAATGGGTAACTCCCGAGAGAGTGTACAGAGCAGGACAGCAAGG
1330 1340 1350 1360 1370 1380

S T Y S L S S T L T L S K A D Y E K H K
ACAGCACCTACAGCCTCAGCAGCACCTGACGCTGAGCAAAGCAGACTACGAGAAACACA
1390 1400 1410 1420 1430 1440

V Y A C E V T H Q G L S S P V T K S F N
AAGTCTACGCCCTGCGAAGTCAACCATCAGGGCCTGAGCTCGCCCGTCAAAAGAGCTTCA
1450 1460 1470 1480 1490 1500

R G E S * * (SEQ ID NO. 188)
ACCGGGAGAGTATAGTAAGAATTC (SEQ ID NO. 189)
1510 1520

Fig.10 d

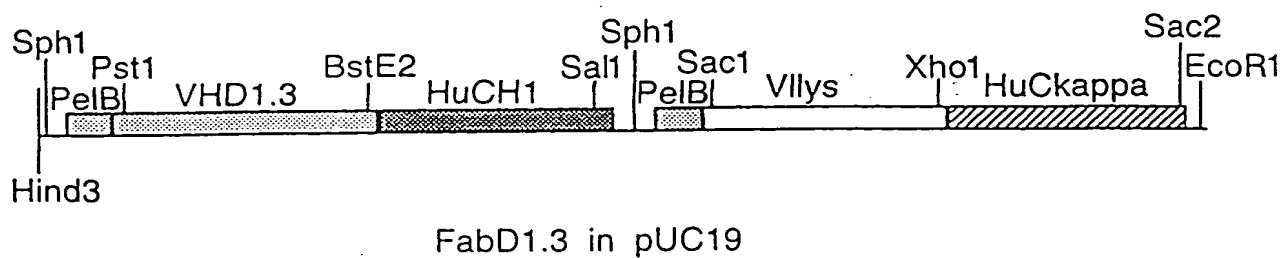


Fig.11.

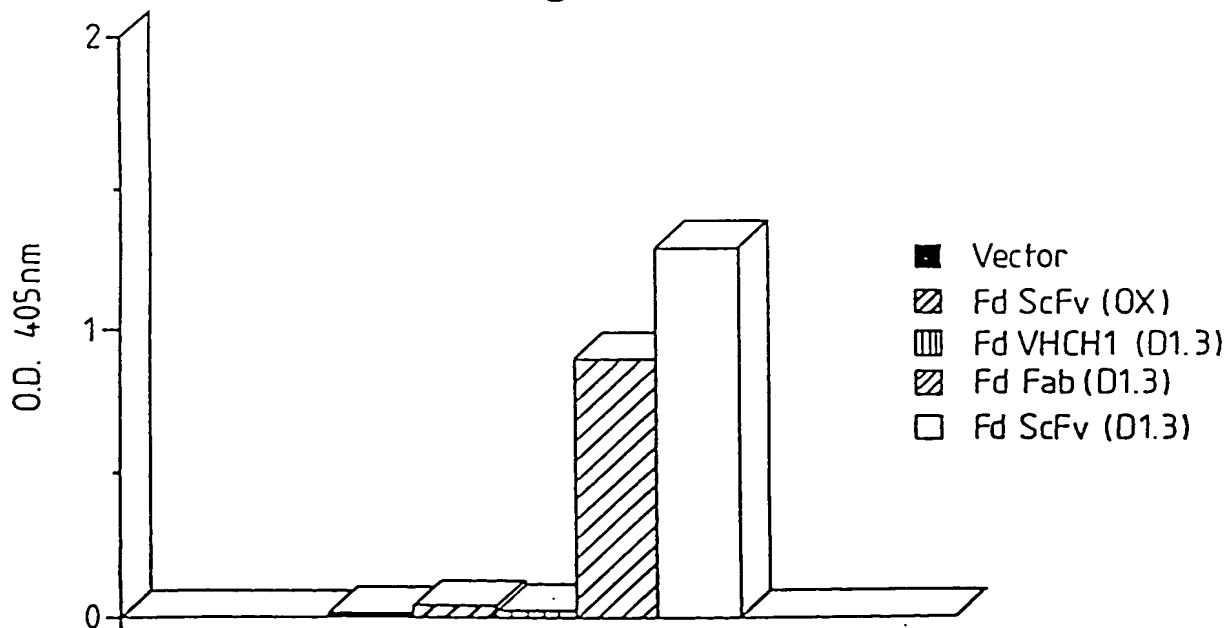




Fig.12a.

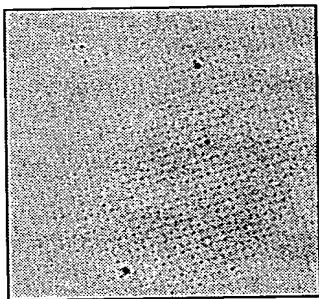


Fig.12b.

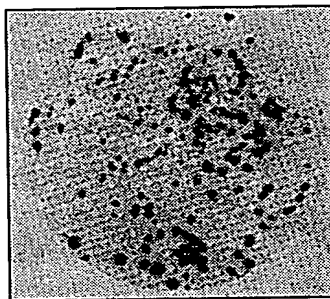




Fig.13.

Q V Q L Q E S G G G L V Q P G G
CAG GTG CAG CTG CAG GAG TCA GGA GGA GGC TTG GTA CAG CCT GGG GGT
PstI
S L R L S C A T S G F T F S N Y
TCT CTG AGA CTC TCC TGT GCA ACT TCT GGG TTC ACC TTC AGT AAT TAC
Y M G W V R Q P P G K A L E W L
TAC ATG GGC TGG GTC CGC CAG CCT CCA GGA AAG GCA CTT GAG TGG TTG
G S V R N K V N G Y T T E Y S A
GGT TCT GTT AGA AAC AAA GTT AAT GGT TAC ACA ACA GAG TAC AGT GCA
S V K G R F T I S R D N F Q S I
TCT GTG AAG GGG CGG TTC ACC ATC TCC AGA GAT AAT TTC CAA AGC ATC
L Y L Q I N T L R T E D S A T Y
CTC TAT CTT CAA ATA AAC ACC CTG AGA ACT GAG GAC AGT GCC ACT TAT
Y C A R G Y D Y G A W F A Y W G
TAC TGT GCA AGA GGC TAT GAT TAC GGG GCC TGG TTT GCT TAC TGG GGC
Q G T L V T v s s g g g g s g g g g s
CAA GGG ACC CTG GTC ACC gtc tcc tca ggtggaggcggttcaggcgagggtggctct
BstEII
g g g g s d i E L T Q T P L S L P V
ggcggtggcggtcgac atc GAG CTC ACC CAA ACT CCA CTC TCC CTG CCT GTC
SacI
S L G D Q A S I S C R S S Q S I
AGT CTT GGA GAT CAA GCC TCC ATC TCT TGC AGA TCT AGT CAG AGC ATT
V H S N G N T Y L E W Y L Q K P
GTA CAT AGT AAT GGA AAC ACC TAT TTA GAA TGG TAC CTG CAG AAA CCA
PstI
G Q S P K L L I Y K V S N R F S
GGC CAG TCT CCA AAG CTC CTG ATC TAC AAA GTT TCC AAC CGA TTT TCT
G V P D R F S G S G S G T D F T
GGG GTC CCA GAC AGG TTC AGT GGC AGT GGA TCG GGG ACA GAT TTC ACA
L K I S R V E A E D L G V Y Y C
CTC AAG ATC AGC AGA GTG GAG GCT GAG GAT CTG GGA GTT TAT TAC TGC
F Q G S H V P Y T F G G G T K L
TTT CAA GGT TCA CAT GTT CCG TAC ACG TTC GGA GGG GGG ACC AAG CTC
E I K R
GAG ATC AAA CGG (SEQ ID NO. 190)
XhoI (SEQ ID NO. 191)

Fig.14.

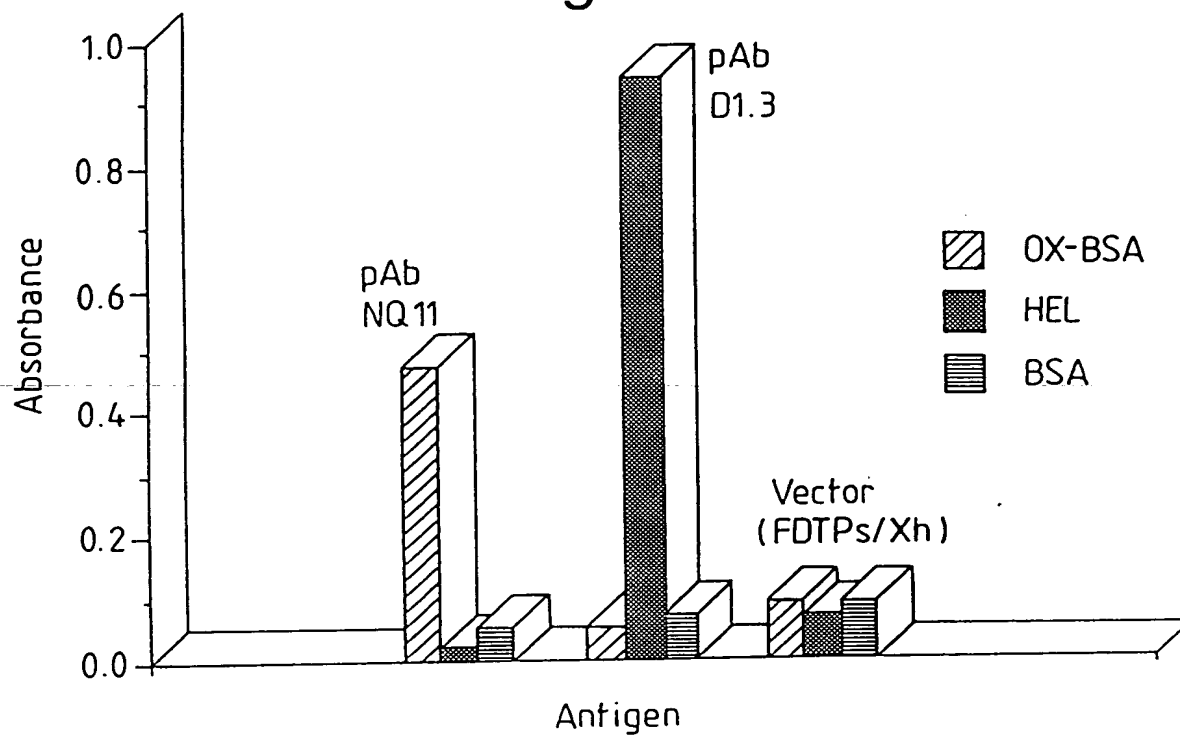


Fig.15.

5' END

TCT CAC AGT GCA CAA ACT GTT GAA CGG ACA CCA GAA ATG CCT GTT CTG (SEQ ID NO:193)
 R T P E M P V L (SEQ ID NO:192)
 ApaL1

3' END

K A A L G L K (SEQ ID NO:194)
 AAA GCC GCT CTG GGG CTG AAA GCG GCC GCA GAA ACT GTT GAA AGT etc. (SEQ ID NO:195)
 Not I

Fig.16a

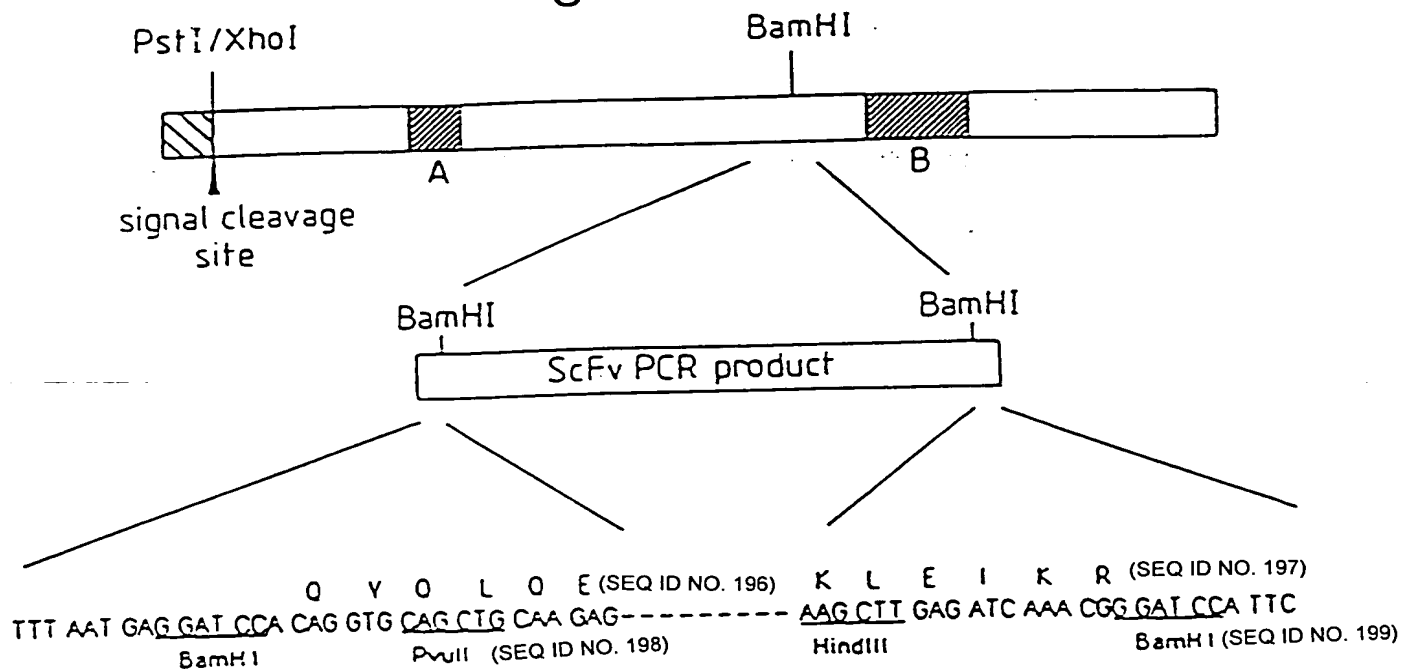


Fig.16b

A (1834) 5' GAG GGT GGT GGC TCT (SEQ ID NO. 200)
 - - -C - - (SEQ ID NO. 201)
 - - -C - - (SEQ ID NO. 202)
 - - -C - - ACT 3' (1839) (SEQ ID NO. 203)

B (2284) 5' - GGC GGC GGC TCT (SEQ ID NO. 204)
 - GGT GGT GGT - (SEQ ID NO. 205)
 - - GGC GGC - (SEQ ID NO. 206)
 GAG - - GGC - (SEQ ID NO. 207)
 - - - GGT - (SEQ ID NO. 208)
 - - - GGC - (SEQ ID NO. 209)
 - - - GGT - (SEQ ID NO. 210)
 - - - GGC - 3' (2379) (SEQ ID NO. 211)

Reverse complement of mutagenic
 oligo G3Bamlink

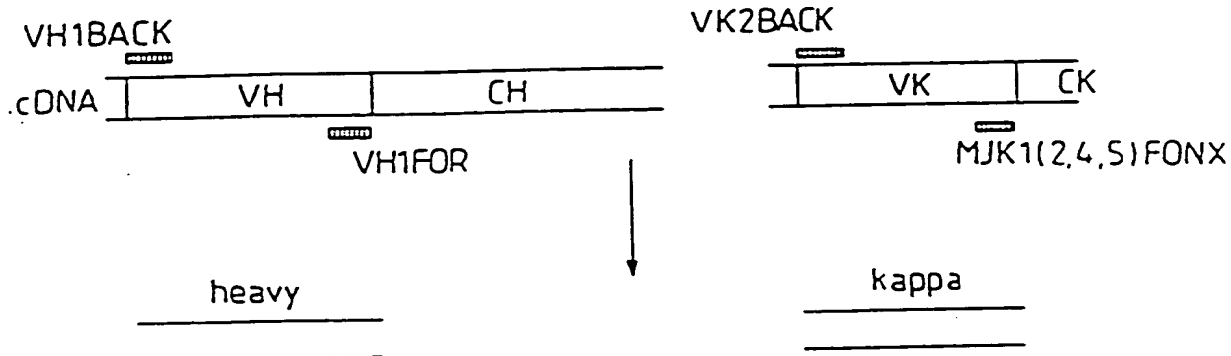
5' GAG GGT GGC GGA TCC (SEQ ID NO. 212)

GAG GGT GGC GG 3' (SEQ ID NO. 213)

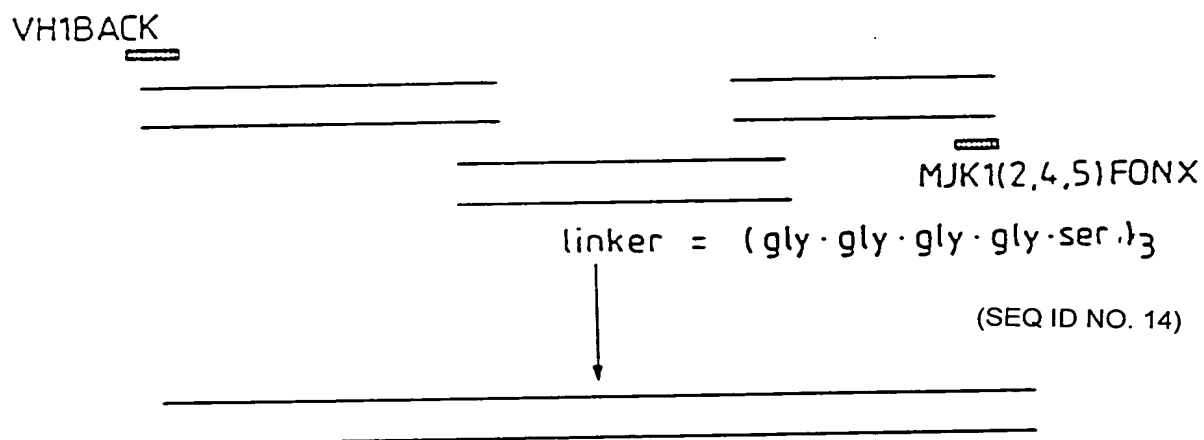


Fig.17.

1) PRIMARY PCR



2) ASSEMBLY PCR



3) ADDING RESTRICTION SITES

VHBKAPA10

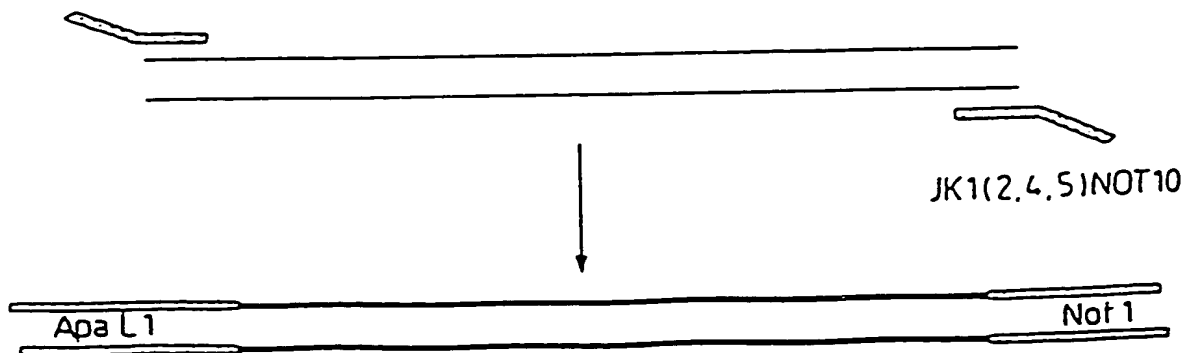




Fig.18.

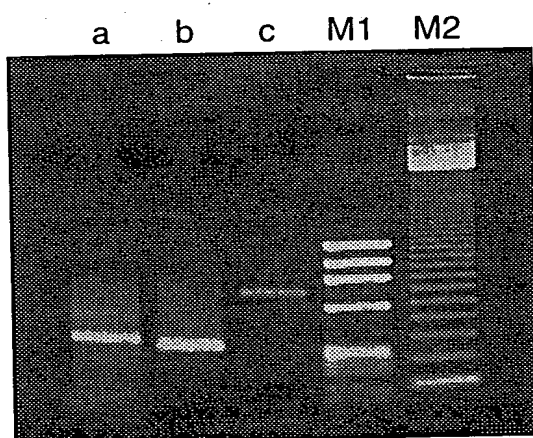


Fig.19.

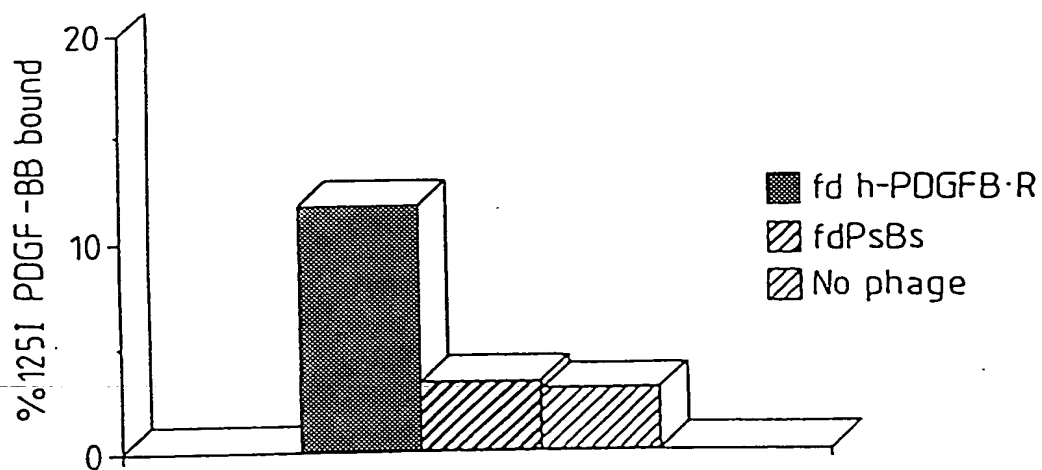


Fig.20.

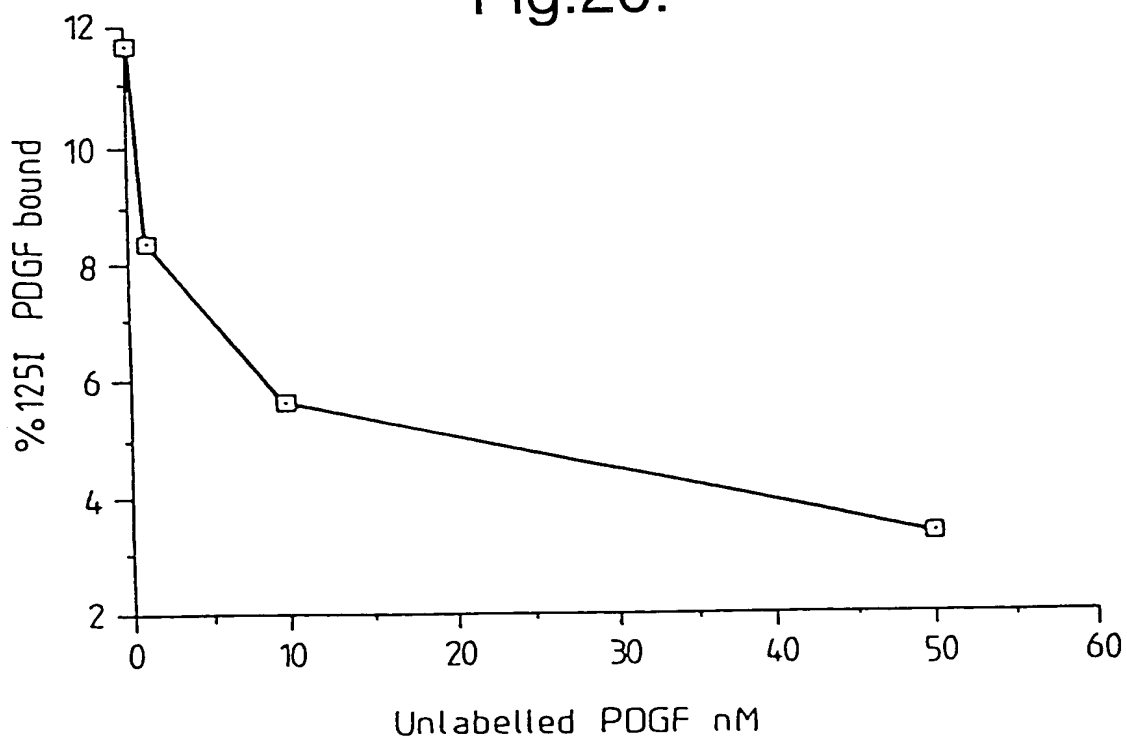


Fig.21.

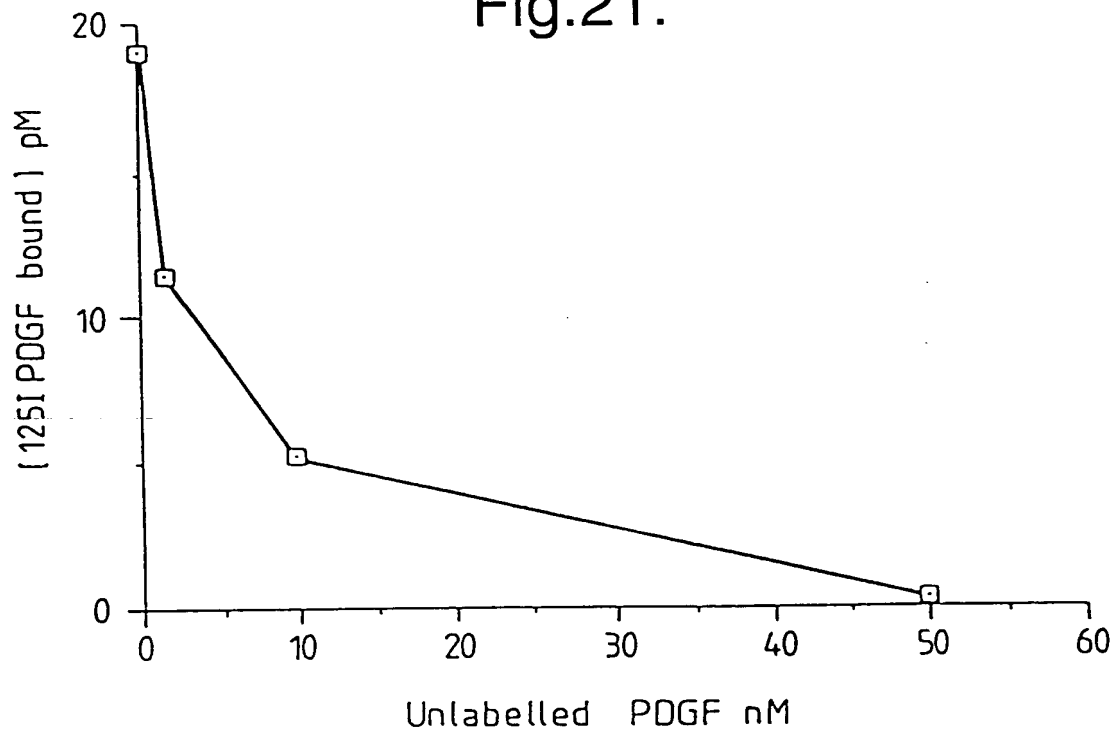


Fig.22.

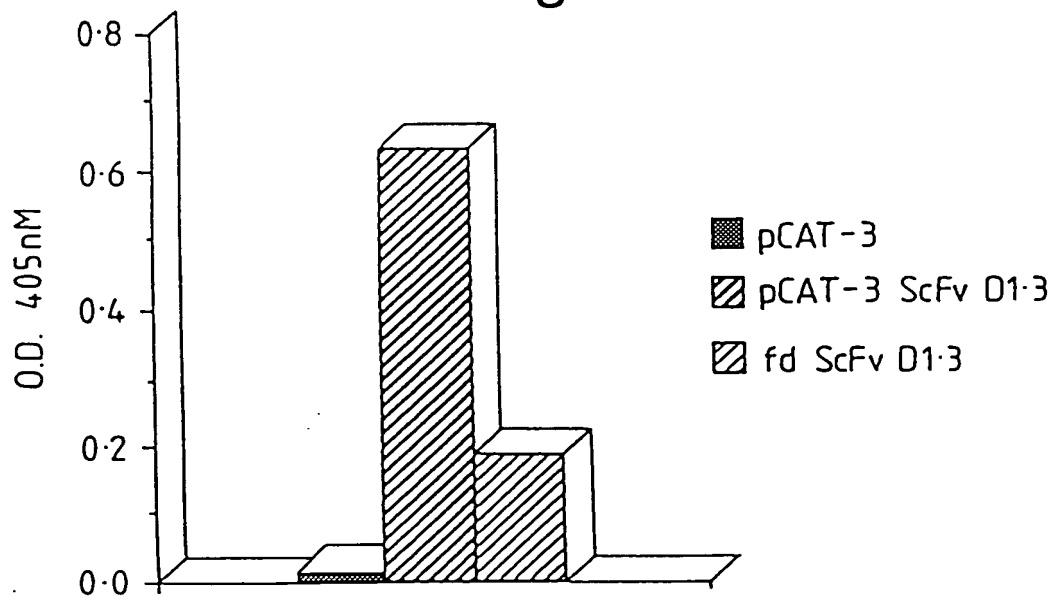




Fig.23a

d
M

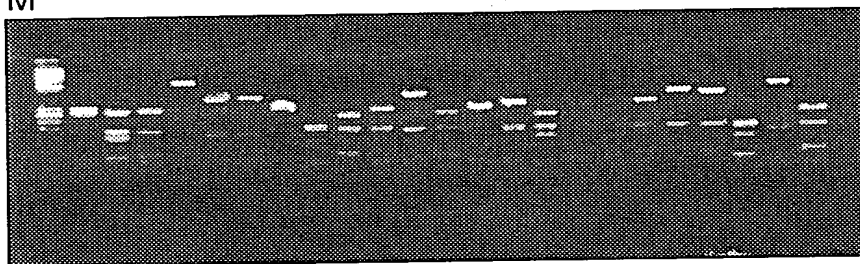


Fig.23b

M

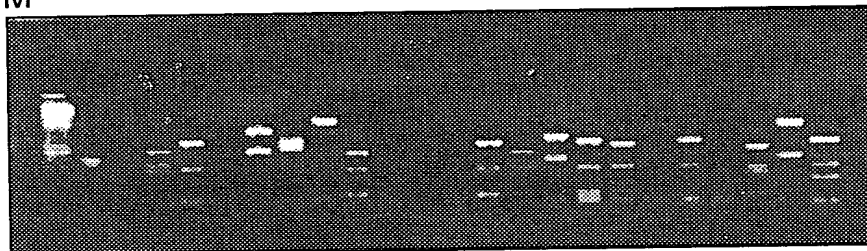




Fig.24a

VH sequences

from combinatorial library:

	CDR1	CDR2	CDR3		
A	QVQLQSGOAEELARPGASVKNHCKASGTTT	YINP56GYTTHNQKFKD	KNTLTADKSSSTAYHQLSSLTSED8AVTYCAR	HCQCTTIVTVS9	x4
B	QVQLQSGOAEELAKPGAEVKNHCKASGTTT	YINP56GYTTHNQKFKD	KNTLTADKSSSTAYHQLSSLTSED8AVTYCAR	HCQCTTIVTVS9	x9
C	QVQLQSGOPELVKPGAGVKNHCKASGTTT	YINP56GYTTHNQKFKD	KNTLTADKSSSTAYHQLSSLTSED8AVTYCAR	HCQCTTIVTVS9	x3
D	QVQLQSGOPELVKPGAGVKNHCKASGTTT	YINP56GYTTHNQKFKD	KNTLTADKSSSTAYHQLSSLTSED8AVTYCAR	HCQCTTIVTVS9	x3
E	QVQLQSGOPELVKPGAGVKNHCKASGTTT	YINP56GYTTHNQKFKD	KNTLTADKSSSTAYHQLSSLTSED8AVTYCAR	HCQCTTIVTVS9	x3
F	QVQLQSGOPELVKPGAGVKNHCKASGTTT	YINP56GYTTHNQKFKD	KNTLTADKSSSTAYHQLSSLTSED8AVTYCAR	HCQCTTIVTVS9	x3
G	QVQLQSGOPELVKPGAGVKNHCKASGTTT	YINP56GYTTHNQKFKD	KNTLTADKSSSTAYHQLSSLTSED8AVTYCAR	HCQCTTIVTVS9	x3
H	QVQLQSGOPELVKPGAGVKNHCKASGTTT	YINP56GYTTHNQKFKD	KNTLTADKSSSTAYHQLSSLTSED8AVTYCAR	HCQCTTIVTVS9	x3

from hierarchical library Vh-rep x Vh-d:

	CDR1	CDR2	CDR3		
I	QVQLQSGOAEELARPGASVKNHCKASGTTT	YINP56GYTTHNQKFKD	KNTLTADKSSSTAYHQLSSLTSED8AVTYCAR	HCQCTTIVTVS9	x4
J	QVQLQSGOAEELAKPGAEVKNHCKASGTTT	YINP56GYTTHNQKFKD	KNTLTADKSSSTAYHQLSSLTSED8AVTYCAR	HCQCTTIVTVS9	x9
K	QVQLQSGOAEELAKPGAGVKNHCKASGTTT	YINP56GYTTHNQKFKD	KNTLTADKSSSTAYHQLSSLTSED8AVTYCAR	HCQCTTIVTVS9	x3
L	QVQLQSGOAEELAKPGAGVKNHCKASGTTT	YINP56GYTTHNQKFKD	KNTLTADKSSSTAYHQLSSLTSED8AVTYCAR	HCQCTTIVTVS9	x3
M	QVQLQSGOAEELAKPGAGVKNHCKASGTTT	YINP56GYTTHNQKFKD	KNTLTADKSSSTAYHQLSSLTSED8AVTYCAR	HCQCTTIVTVS9	x3
N	QVQLQSGOAEELAKPGAGVKNHCKASGTTT	YINP56GYTTHNQKFKD	KNTLTADKSSSTAYHQLSSLTSED8AVTYCAR	HCQCTTIVTVS9	x3
O	QVQLQSGOAEELAKPGAGVKNHCKASGTTT	YINP56GYTTHNQKFKD	KNTLTADKSSSTAYHQLSSLTSED8AVTYCAR	HCQCTTIVTVS9	x3
P	QVQLQSGOAEELAKPGAGVKNHCKASGTTT	YINP56GYTTHNQKFKD	KNTLTADKSSSTAYHQLSSLTSED8AVTYCAR	HCQCTTIVTVS9	x3
Q	QVQLQSGOAEELAKPGAGVKNHCKASGTTT	YINP56GYTTHNQKFKD	KNTLTADKSSSTAYHQLSSLTSED8AVTYCAR	HCQCTTIVTVS9	x3
R	QVQLQSGOAEELAKPGAGVKNHCKASGTTT	YINP56GYTTHNQKFKD	KNTLTADKSSSTAYHQLSSLTSED8AVTYCAR	HCQCTTIVTVS9	x3
S	QVQLQSGOAEELAKPGAGVKNHCKASGTTT	YINP56GYTTHNQKFKD	KNTLTADKSSSTAYHQLSSLTSED8AVTYCAR	HCQCTTIVTVS9	x3
T	QVQLQSGOAEELAKPGAGVKNHCKASGTTT	YINP56GYTTHNQKFKD	KNTLTADKSSSTAYHQLSSLTSED8AVTYCAR	HCQCTTIVTVS9	x3
U	QVQLQSGOAEELAKPGAGVKNHCKASGTTT	YINP56GYTTHNQKFKD	KNTLTADKSSSTAYHQLSSLTSED8AVTYCAR	HCQCTTIVTVS9	x3
V	QVQLQSGOAEELAKPGAGVKNHCKASGTTT	YINP56GYTTHNQKFKD	KNTLTADKSSSTAYHQLSSLTSED8AVTYCAR	HCQCTTIVTVS9	x3



Fig. 24b

Vx sequences

from combinatorial library:

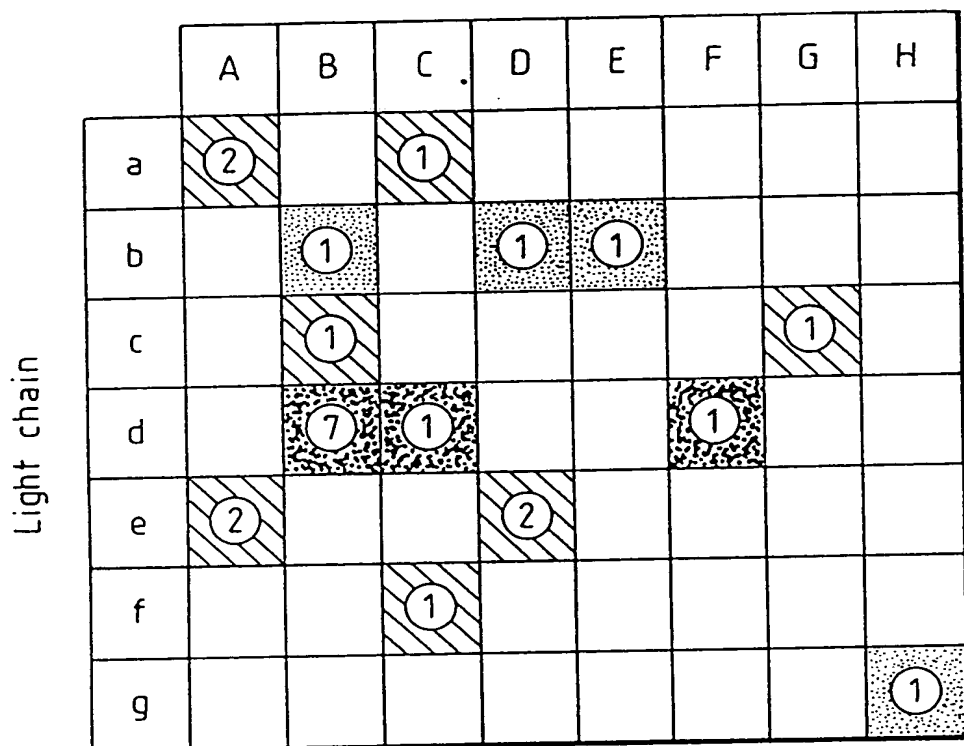
	COR1	COR2	COR3			
a	DIELTQSP5SLASLGERVSLTC	WLOQKPGSIPKRLIY	QVPRFSGSGSGTSGTSLTISSEEDVATTC	FGAGTKLEIKRA x3	V	ox-1ike (SEQ ID NO. 236)
b	DIELTQSPAIMSASPGKVTTC	MYQOKPGSPKVMIIY	QVPRFSGSGTSGTSGTSLTISSEEDVATTC	FGAGTKLEIKRA x3	IV	ox-1ike (SEQ ID NO. 237)
c	DIELTQSPPTTHAASPGKVTTC	MYQOKPGSPKLLIY	QVPRFSGSGTSGTSGTSLTIGTHEAEDVATTC	FGAGTKLEIKRA x3	IV	ox-1ike (SEQ ID NO. 238)
d	DIELTQSPPTTHAASPGKVTTC	MYQOKPGSPKLLIS	QVPRFSGSGTSGTSGTSLTIGTHEAEDVATTC	FGAGTKLEIKRA x9	IV	ox-1ike (SEQ ID NO. 239)
e	DIELTQSPPTTHAASPGKVTTC	MYQOKPGSPKLMIIY	QVPRFSGSGTSGTSGTSLTISSEEDVATTC	FGAGTKLEIKRA x4	VI	ox-1ike? (SEQ ID NO. 240)
f	DIELTQSPPTTHAASPGKVTTC	MYQOKPGSPKRMIIY	QVPRFSGSGTSGTSGTSLTISSEEDVATTC	FGAGTKLEIKRA	VI	Wox1 (SEQ ID NO. 241)
g	DIELTQSPPTTHAASPGKVTTC	MYQOKPGSPKRMIIY	QVPRFSGSGTSGTSGTSLTISSEEDVATTC	FGAGTKLEIKRA	VI	ox-1ike? (SEQ ID NO. 242)

from hierarchical library VII-B x Vx-rep:

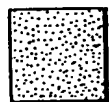
h	DIELTQSPAIMSASPGKVTTC	SASSSVSTMI	QVPRFSGSGTSGTSGTSLTISSEEDVATTC	FGAGTKLEIKRA x4	IV/VI	Wox1 (SEQ ID NO. 243)
i	DIELTQSPPTTHAASPGKVTTC	SASSSVSTMI	QVPRFSGSGTSGTSGTSLTISSEEDVATTC	FGAGTKLEIKRA	V	ox-1ike? (SEQ ID NO. 244)
j	DIELTQSPPTTHAASPGKVTTC	SASSSVSTMI	QVPRFSGSGTSGTSGTSLTIGTHEAEDVATTC	FGAGTKLEIKRA	V	ox-1ike (SEQ ID NO. 245)
k	DIELTQSPPTTHAASPGKVTTC	SASSSVSTMI	QVPRFSGSGTSGTSGTSLTIGTHEAEDVATTC	FGAGTKLEIKRA	V	ox-1ike (SEQ ID NO. 246)
l	DIELTQSPPTTHAASPGKVTTC	SASSSVSTMI	QVPRFSGSGTSGTSGTSLTIGTHEAEDVATTC	FGAGTKLEIKRA	V	ox-1ike (SEQ ID NO. 247)
m	DIELTQSPPTTHAASPGKVTTC	SASSSVSTMI	QVPRFSGSGTSGTSGTSLTIGTHEAEDVATTC	FGAGTKLEIKRA	V	ox-1ike (SEQ ID NO. 248)
n	DIELTQSPPTTHAASPGKVTTC	SASSSVSTMI	QVPRFSGSGTSGTSGTSLTIGTHEAEDVATTC	FGAGTKLEIKRA	V	ox-1ike (SEQ ID NO. 249)
o	DIELTQSPPTTHAASPGKVTTC	SASSSVSTMI	QVPRFSGSGTSGTSGTSLTIGTHEAEDVATTC	FGAGTKLEIKRA x3	V	ox-1ike (SEQ ID NO. 250)
p	DIELTQSPPTTHAASPGKVTTC	SASSSVSTMI	QVPRFSGSGTSGTSGTSLTIGTHEAEDVATTC	FGAGTKLEIKRA x3	IV/VI	Wox1 (SEQ ID NO. 251)
q	DIELTQSPPTTHAASPGKVTTC	SASSSVSTMI	QVPRFSGSGTSGTSGTSLTIGTHEAEDVATTC	FGAGTKLEIKRA	IV/VI	Wox1 (SEQ ID NO. 252)
r	DIELTQSPPTTHAASPGKVTTC	SASSSVSTMI	QVPRFSGSGTSGTSGTSLTIGTHEAEDVATTC	FGAGTKLEIKRA	IV/VI	Wox1 (SEQ ID NO. 253)
s	DIELTQSPPTTHAASPGKVTTC	SASSSVSTMI	QVPRFSGSGTSGTSGTSLTIGTHEAEDVATTC	FGAGTKLEIKRA	IV/VI	ox-1ike (SEQ ID NO. 254)
t	DIELTQSPPTTHAASPGKVTTC	SASSSVSTMI	QVPRFSGSGTSGTSGTSLTIGTHEAEDVATTC	FGAGTKLEIKRA	IV/VI	ox-1ike (SEQ ID NO. 255)
u	DIELTQSPPTTHAASPGKVTTC	SASSSVSTMI	QVPRFSGSGTSGTSGTSLTIGTHEAEDVATTC	FGAGTKLEIKRA	IV/VI	ox-1ike (SEQ ID NO. 256)
v	DIELTQSPPTTHAASPGKVTTC	SASSSVSTMI	QVPRFSGSGTSGTSGTSLTIGTHEAEDVATTC	FGAGTKLEIKRA	IV/VI	ox-1ike (SEQ ID NO. 257)
w	DIELTQSPPTTHAASPGKVTTC	SASSSVSTMI	QVPRFSGSGTSGTSGTSLTIGTHEAEDVATTC	FGAGTKLEIKRA	IV/VI	ox-1ike (SEQ ID NO. 258)

Fig.25.

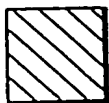
HEAVY CHAIN



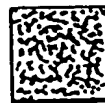
OD_{405nm} in ELISA



0.2-0.9



0.9-2.0



>2.0



Fig.26(a).

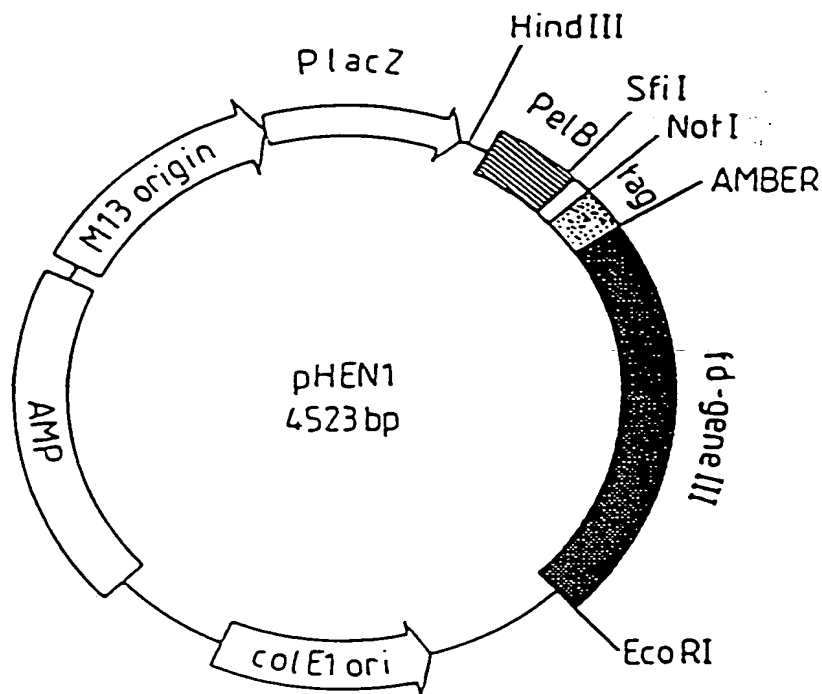


Fig.26(b).

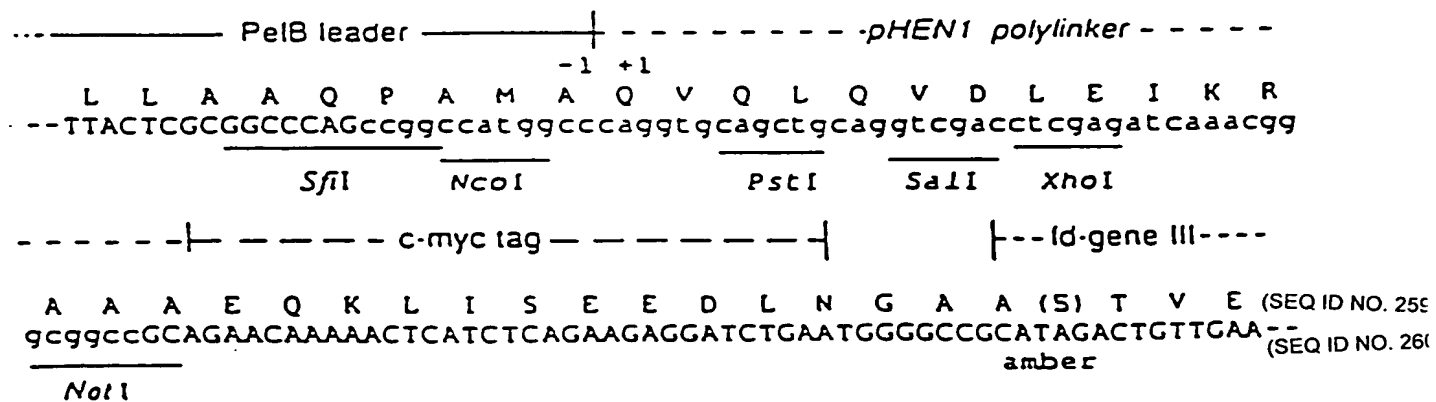


Fig.27.

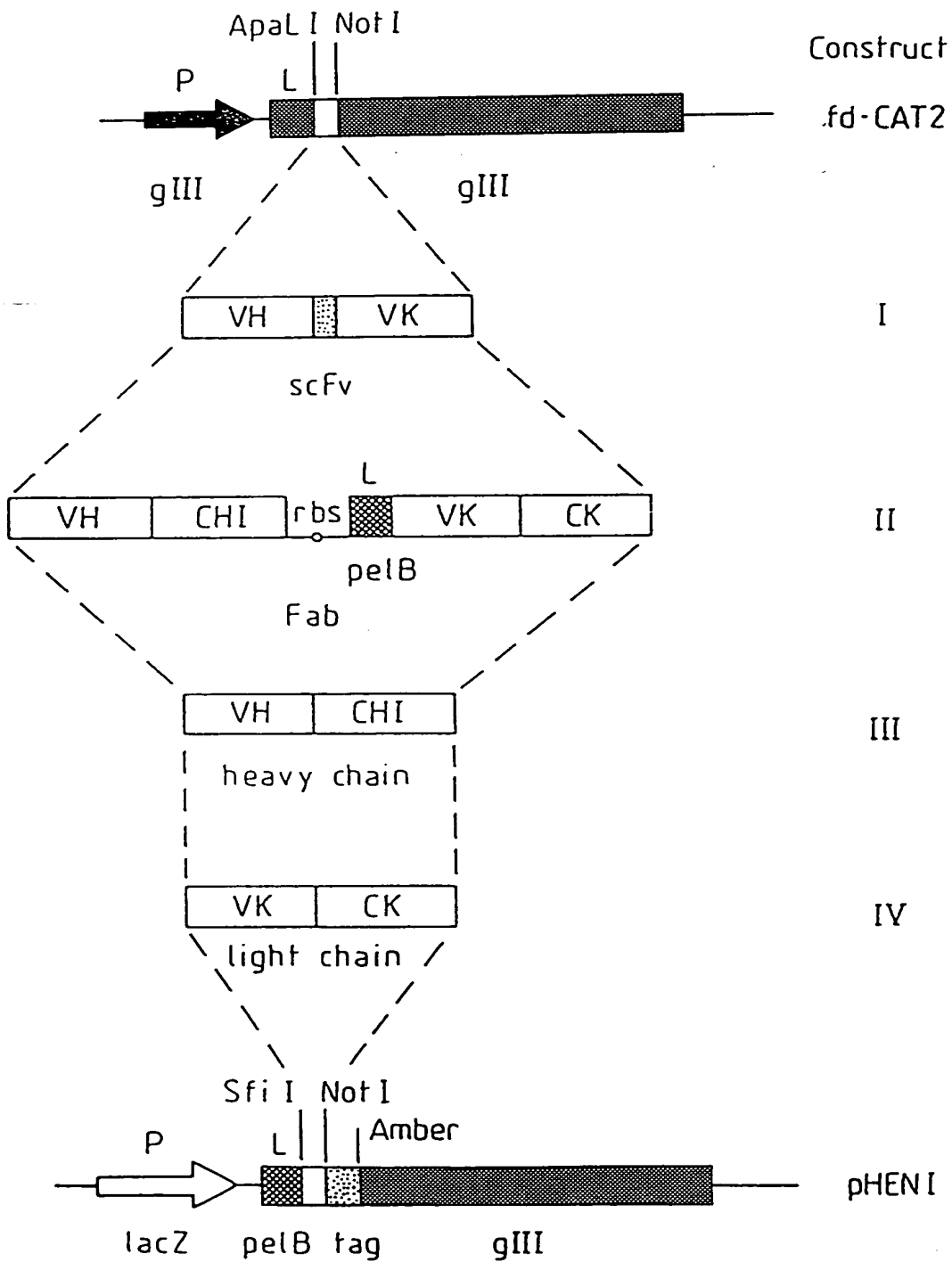


Fig.28.

Fab

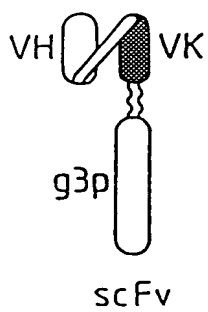
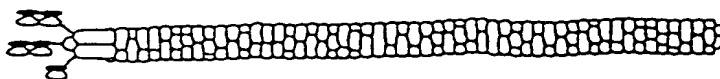
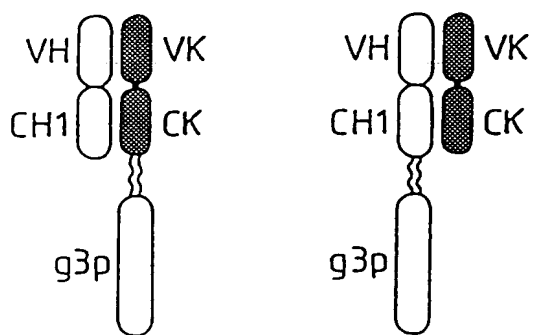




Fig.29.

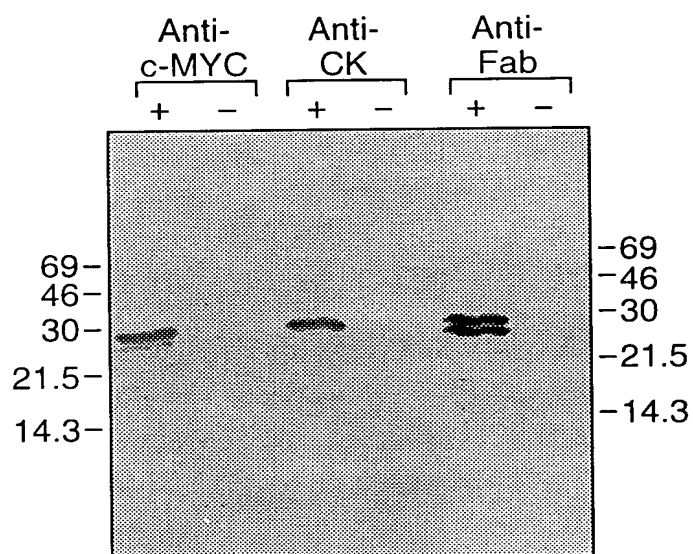




Fig.30.

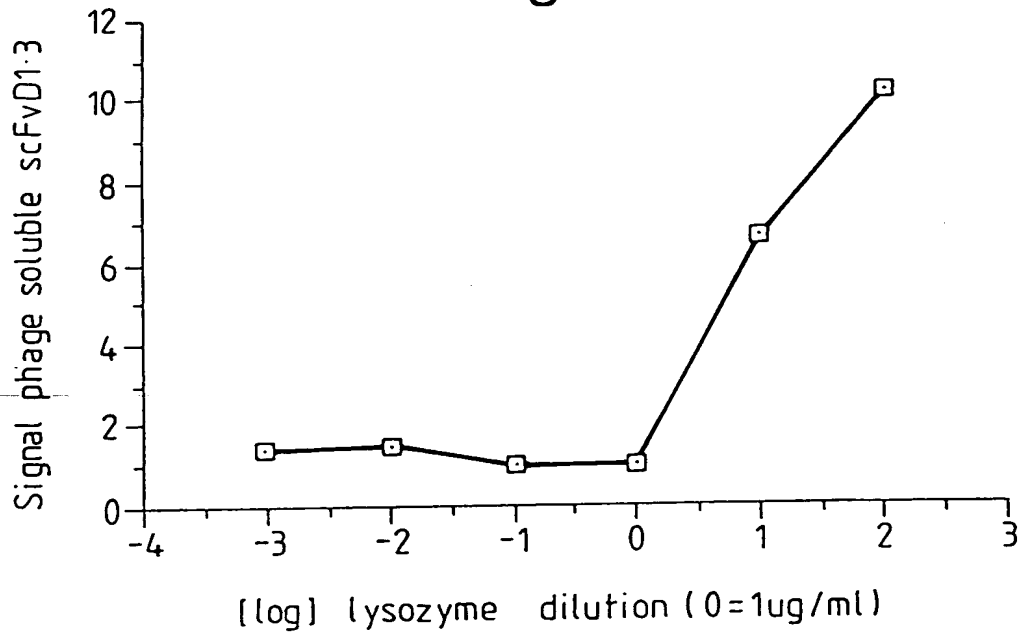


Fig.31.

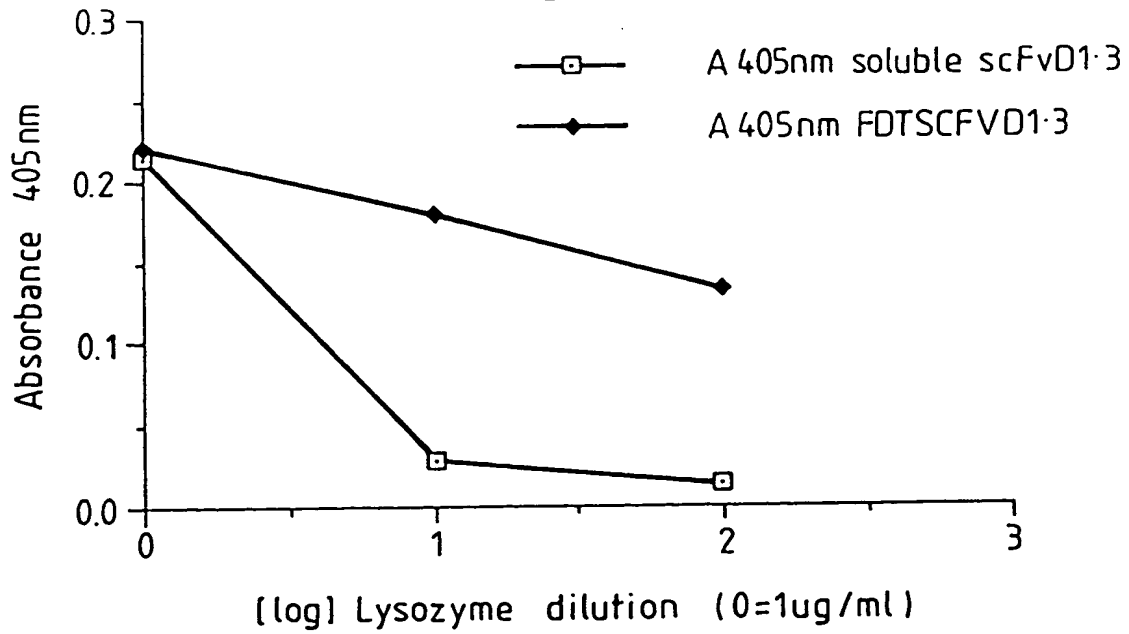


Fig.32.

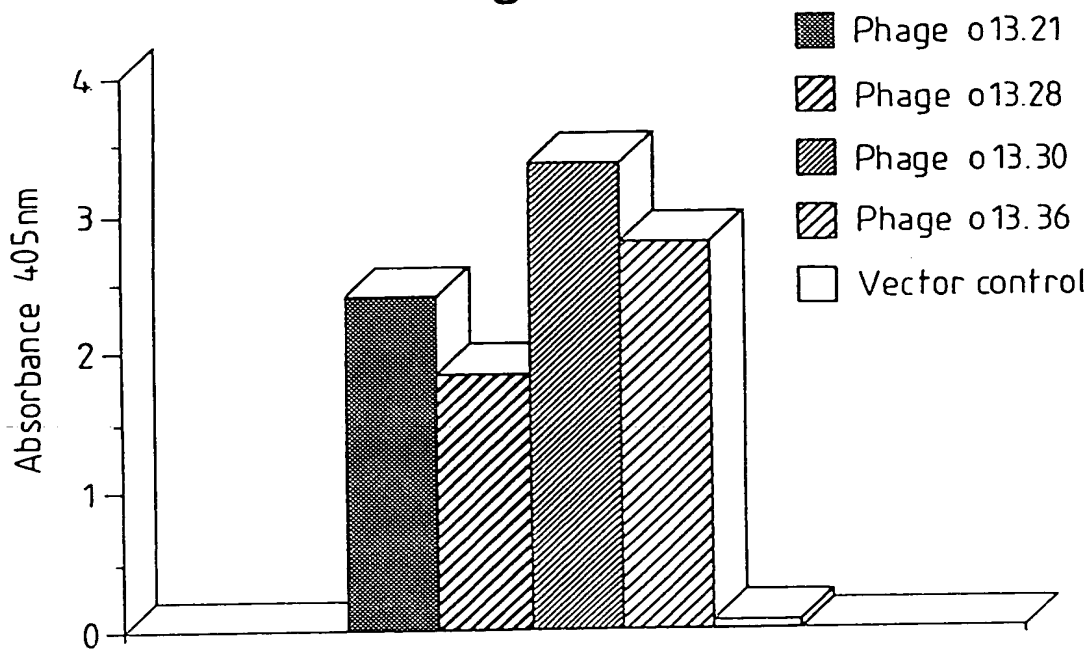


Fig.33.

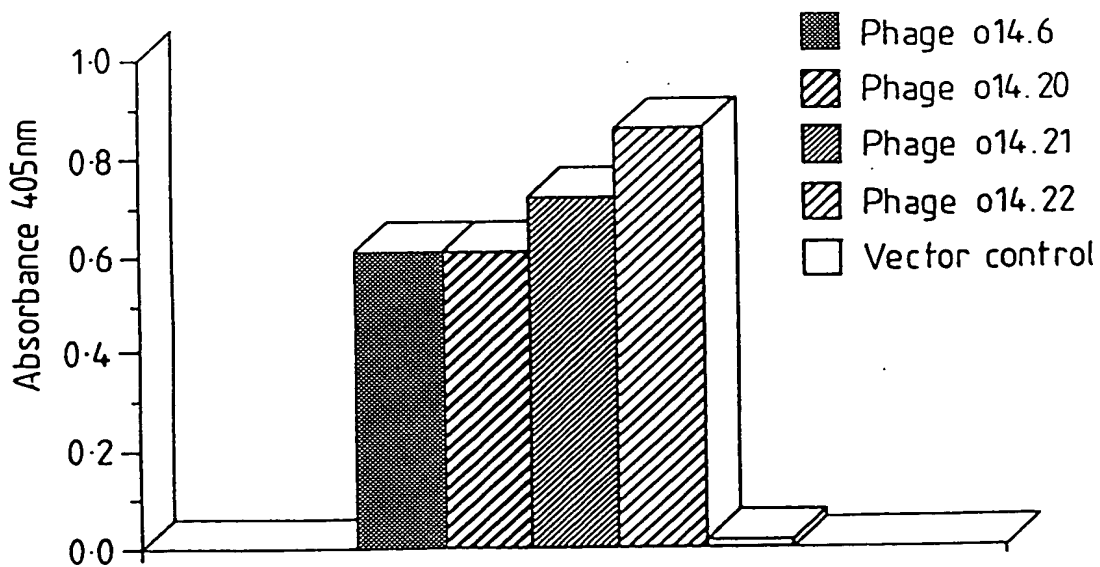




Fig.34.

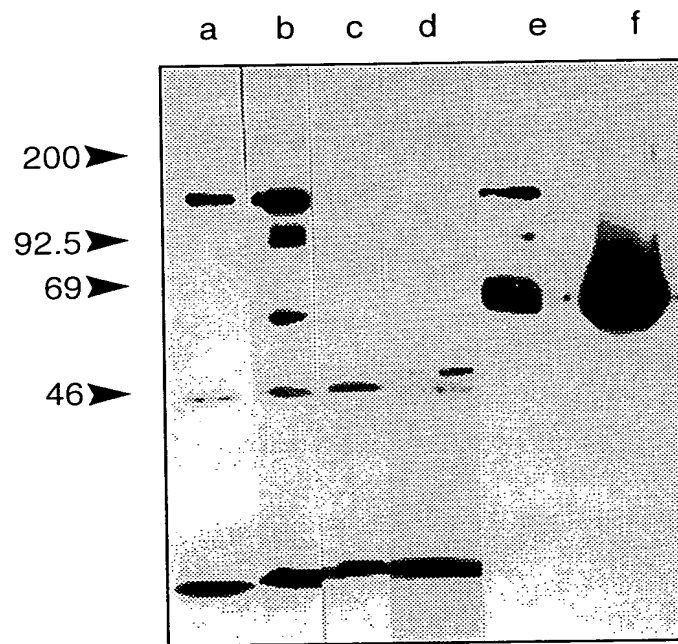


Fig.35A.

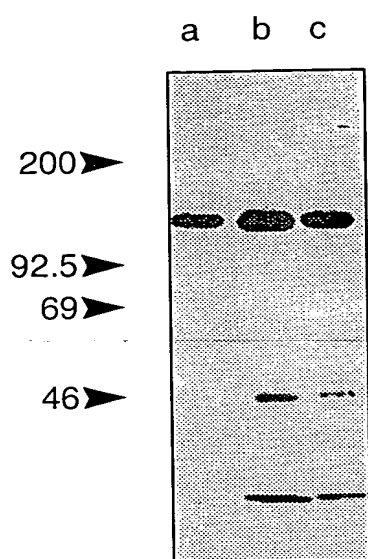


Fig.35B.

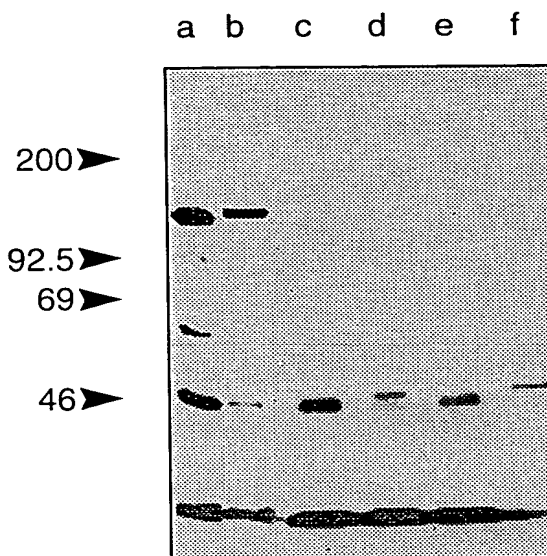


Fig.36.

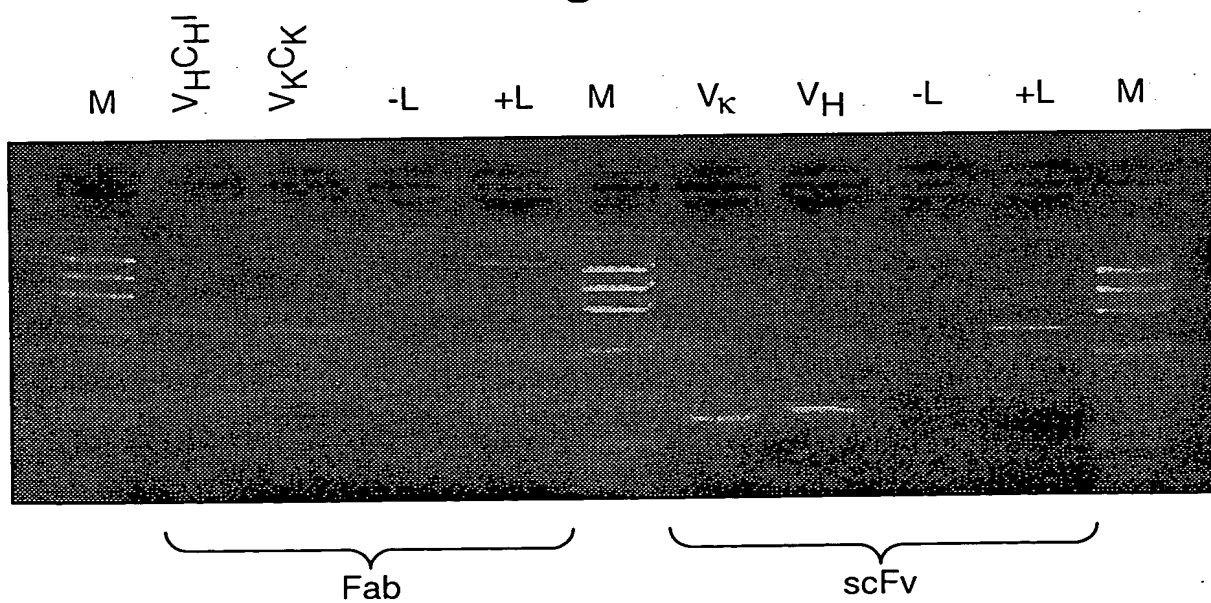


Fig.37.

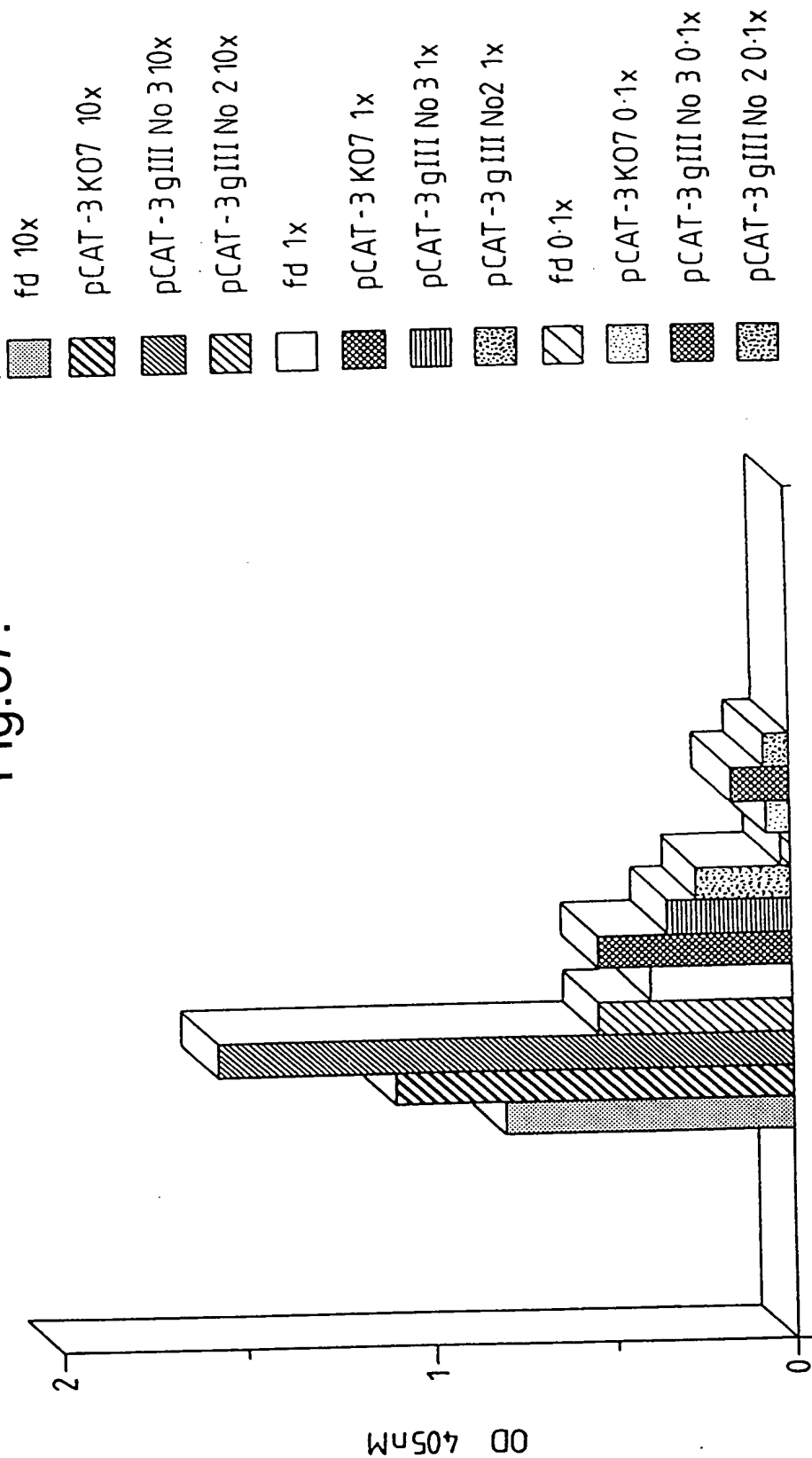




Fig.38A.

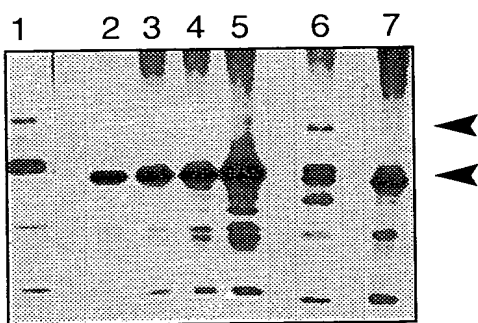


Fig.38B.

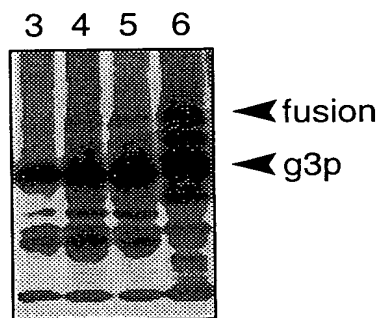


Fig.39.

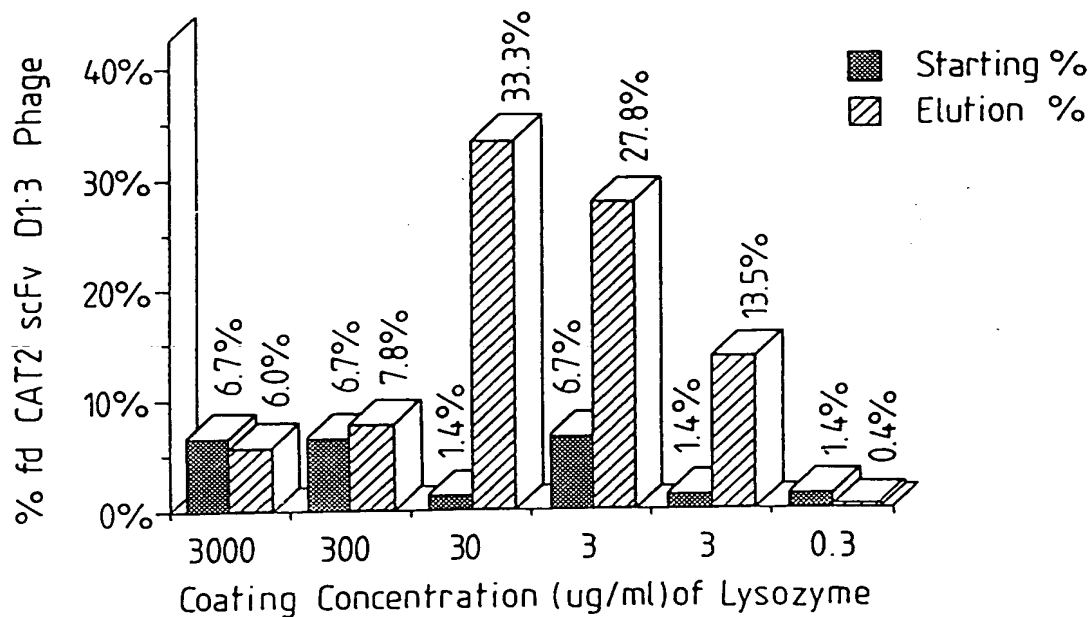


Fig.40.

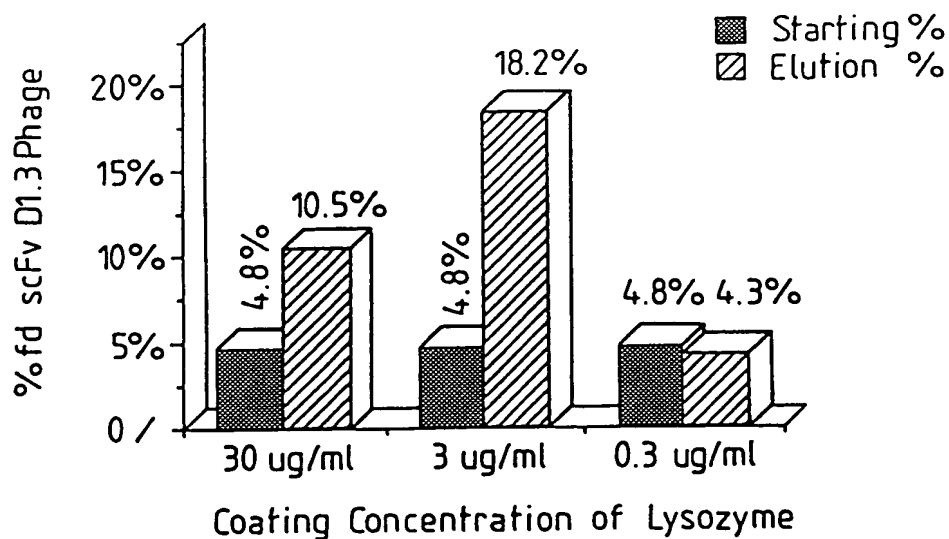




Fig.43.

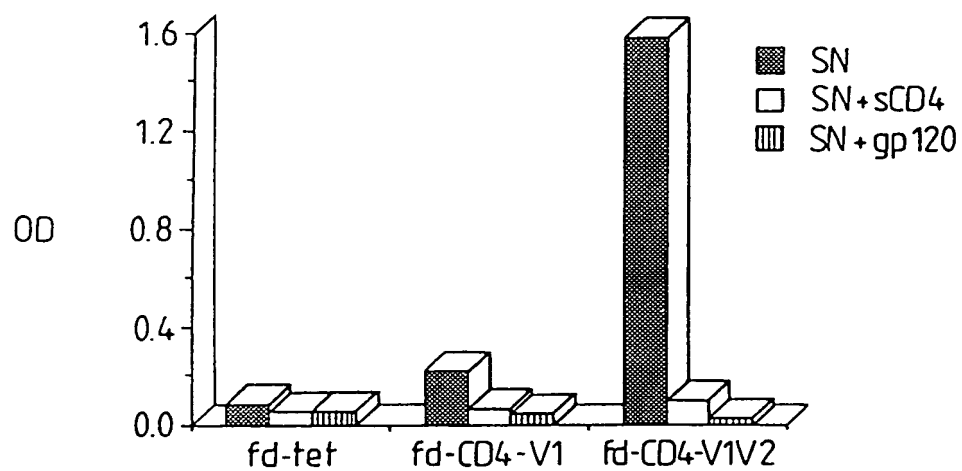




Fig. 44a

10 20 30 40 50 60 70 80 90
TTCTATTCTCACAGTGCCAGGTCCAGCTGCAGCAGTCTGGGGCTGAGCTTGTGAAGCCCTGGGGCTTCAGTGAAGCTGTCCCTGCAAGGCT
AAGATAAGAGTGTACGTGTCAGGTCGACGCTCGTACAGACCCGACTCGAACACTTCGGACCCCGAAGTCACTTCGACACGACGTTCCGA
PheTyrSerHisSerAlaGlnValGlnLeuGlnSerGlyAlaGluLeuValLysProGlyAlaSerValLysLeuSerCysLysAla
100 110 120 130 140 150 160 170 180
TCTGGCTACACCTTCACCAGCTACTGGATGCACCTGGGTGAAGCAGAGCCCTGGACGAGCCCTTGAGTGGATTGGAAGGATTGATCCTAAT
AGACCGATGTGGAGTGGTCGATGACCTACGTGACCCACTTCGTCTCCGGACCTGCTCCGGAACCTCACCTAACCTTCCTAAGTACAGGATTA
SerGlyTyrThrPheThrSerTyrTrpMetHisTrpValLysGlnArgProGlyArgGlyLeuGluTrpIleGlyArgIleAspProAsn
190 200 210 220 230 240 250 260 270
AGTGGTGGTACTAAGTACAATGAGAAGTTCAAGAGAGCAAGGCCACACTGACTGTAGACAAACCCCTCCAGCACAGCCCTACATGCAGCTCAGC
TCACCACCATGATTCACTTCAAGTCTCGTTCGGTGTGACTGACATCTGTTGGGAGGTCGTGCGGATGTACGTCGAGTCG
SerGlyGlyThrLysTyrAsnGluLysPheLysSerLysAlaThrLeuThrValAspLysProSerSerThrAlaTyrMetGlnLeuSer
280 290 300 310 320 330 340 350 360
AGCCTGACATCTGAGGACTCTGCGGTCTATTATTGTGCAAGATACGACTACGGTAGTAGTACTACTTTGACTACTGGGGCCCAAGGGACC
TCGGACTGTAGACTCCTGAGACGCCAGATAATAACAGTTCTATGCTGATGCCATCATCGATGATGAAGTATGATGACCCCGGTTCCCTGG
SerLeuThrSerGluAspSerAlaValTyrTyrCysAlaArgTyrAspTyrGlySerSerTyrTyrPheAspTyrTrpGlyGlnGlyThr
370 380 390 400 410 420 430 440 450
ACGGTCACCGTCTCCTCAGGTGGAGGCGGTTACGGCGGAGGTGGCTCTGGCGGTGGCGGATCCAGGCTGTTGGGACACACAGGAATCTGCA
TGCCAGTGGCAGAGGAGTCCACCTCCGCCAAGTCCGCCCTCCACCGAGACCCGCCACCGCTAGGGTCCGACAACTGCTGTCTTAGACGT
ThrValThrValSerSerGlyGlyGlySerGlyGlyGlySerGlyGlyGlySerGlnAlaValGlyThrGlnGluSerAla
460 470 480 490 500 510 520 530 540
CTCACCATCACCTGGTGAACAGTACACTCACTTGTCCGCTCAAGTACTGGGGCTGTACAACTAGTAACTATGCCAACTGGGTCCCAA
GAGTGGTGTAGTGACCACTTGTGAGTGAGTGAACAGCGAGTTTCATGACCCCGACAAATGTTGATCATTTGATACGTTGACCCAGGTT
LeuThrThrSerProGlyGluThrValThrLeuThrCysArgSerSerThrGlyAlaValThrThrSerAsnTyrAlaAsnTrpValGln
550 560 570 580 590 600 610 620 630
GAAAAACAGATCATTTATTCACTGGTCTAATAGGTGGTACCAACAACCGAGCTCCAGGTGTTCTCGCCAGATTCTCAGGCTCCCTGATT
CTTTTGGTCTAGTAAATAAGTGACCAAGATTATCCACCATGGTTGTTGGCTCGAGGTCCACAAGGACGGTCTAAGAGTCCGAGGACTAA
GluLysProAspHisLeuPheThrGlyLeuIleGlyGlyThrAsnAsnArgAlaProGlyValProAlaArgPheSerGlySerLeuIle



Fig.44 b

640 650 660 670 680 690 700 C G 710 720
GGAGACAAGGCTGCCCTCACCATCACAGGGGCACAGACTGAGGATGAGGCATATATTTCTGTGCTCTATGGTACAGCAACCATTTGGGTG
CCTCTGTTCCGACGGGAGTGAGTGTCCTCCCGTGCTGACTCCTACTCCGTTATATAAGACACGAGATACCATGTGCTGTTGGTAACCCAC
GlyAspLysAlaAlaLeuThrIleThrGlyAlaGlnThrGluAspGluAlaIleTyrPheCysAlaLeuTrpTyrnberAsnHisTrpVal
730 740 750 760 770
TTCGGTGGAGGAAACAAGTACTGACTGTCCCTCGAGATCANAACGGGGCGGCCGC (SEQ ID NO. 261)
AAGCCACCTCCTTGTTGACTGACAGGAGCTCTAGTTGCCCGCCGGCG
pheGlyGlyGlyThrLysLeuThrValLeuGluIleLysArgAlaAla (SEQ ID NO. 262)

Fig.45.

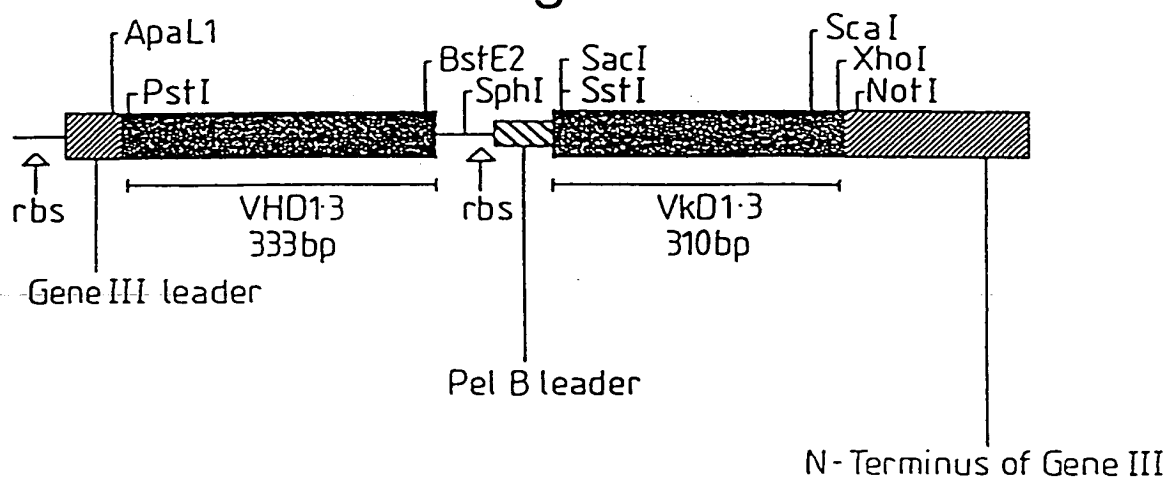


Fig.46.

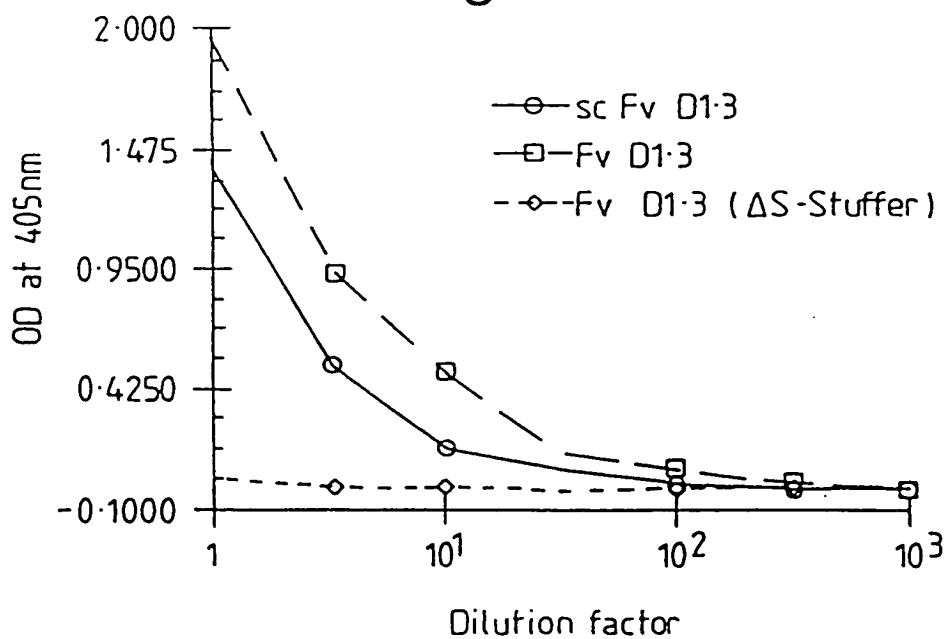


Fig.47.

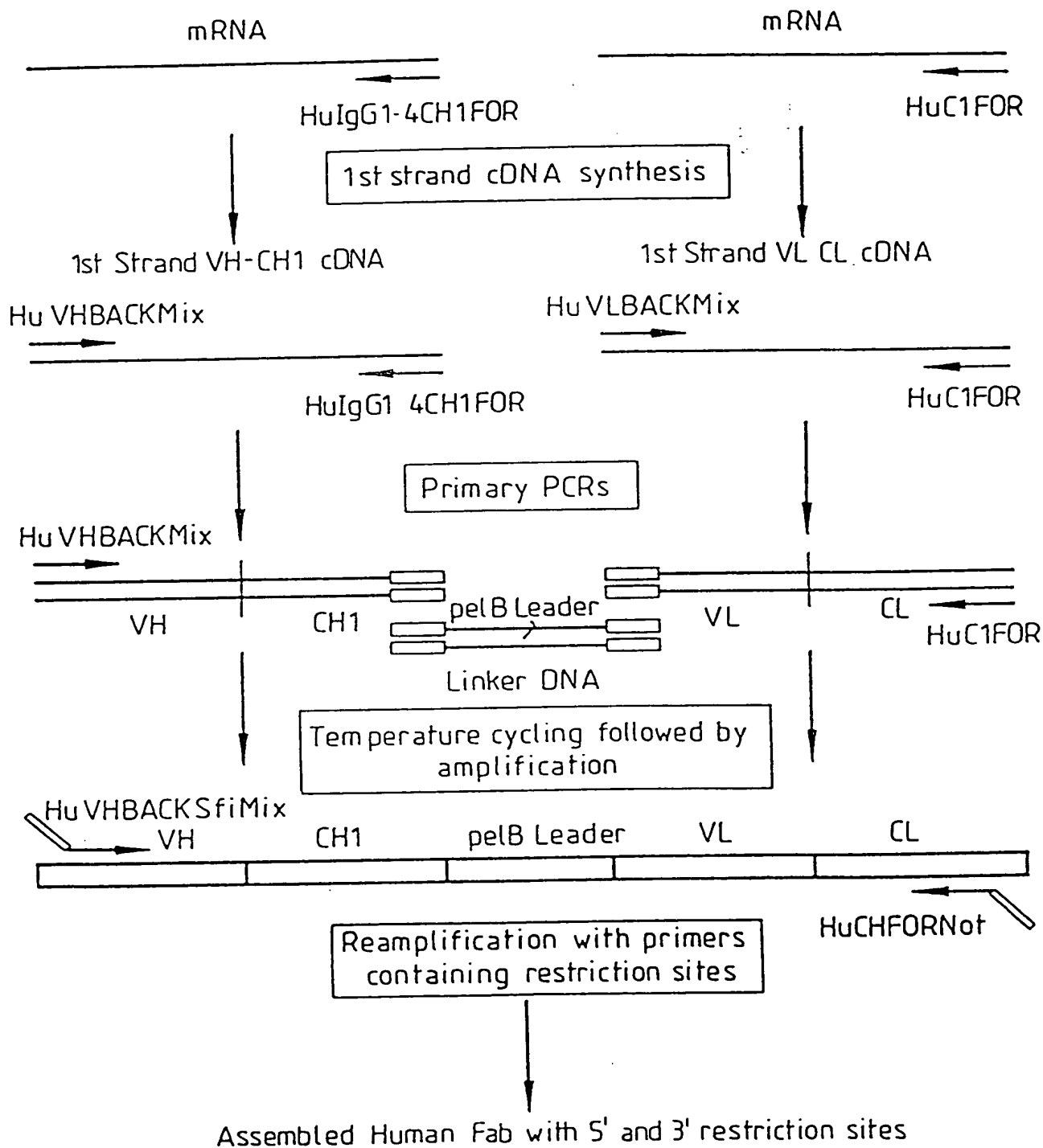


Fig. 48a

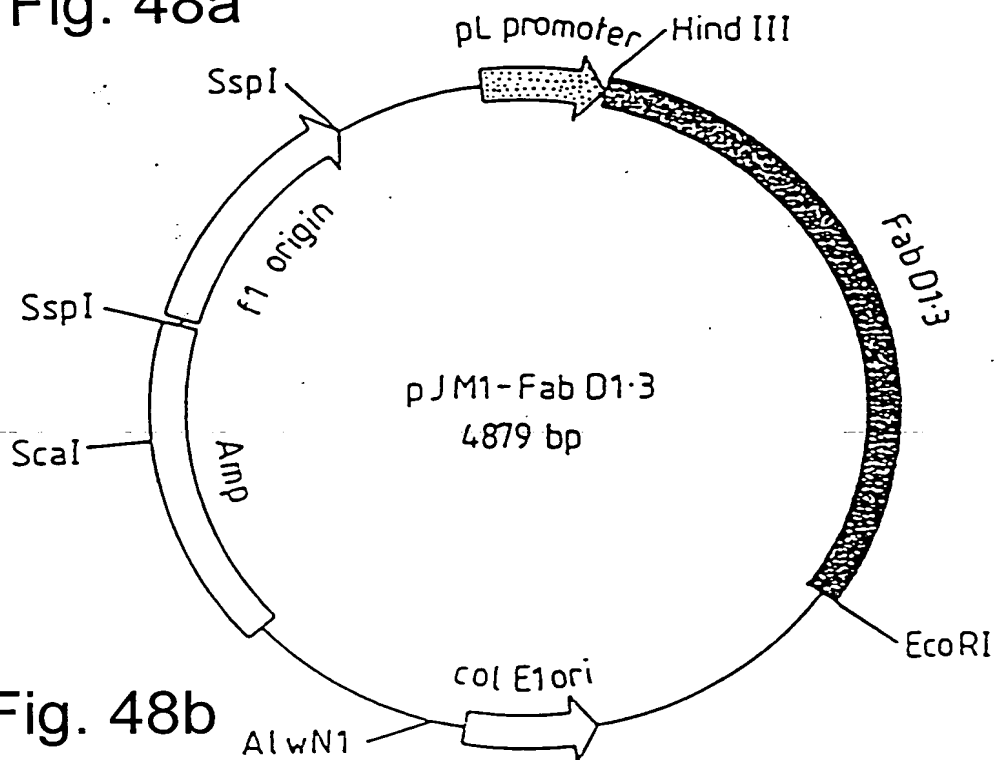


Fig. 48b

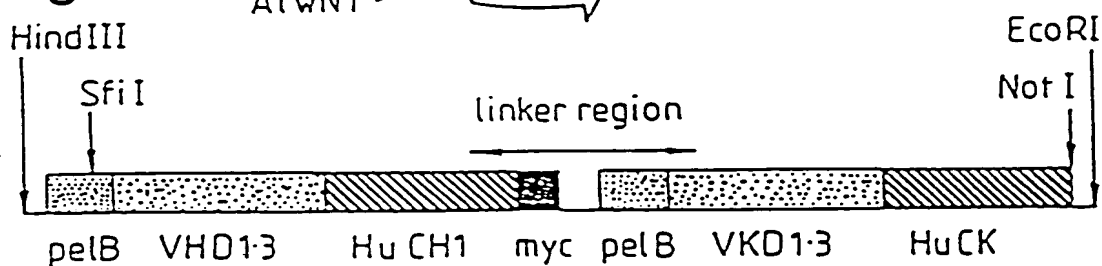


Fig. 48c

← 3' Human CH1 and hinge →
K P S N T K V D K K V E P K S S T K T H T
A A C C C C A G C A A C A C C A A G G T C G A C A A G A A G T T G A G C C C A A T C T T C A A C T A A G A C G C A C A C A

→ myc peptide tag →
S G G E Q K L I S E E D L N * *
T C A G G A G G T G A C A G A G C T C A T C T C A G A G A G G A T C T G A A T T A A T A A G G G A G C T T G C A T G C A

(SEQ ID NO. 263)

← pelB leader →
M K Y L L P T A A A G L
A A T T C T A T T T C A A G G A G A C A G T C A T A A T G A A T A C C T A T T G C C T A C G G C A G C C G T G G A T T G T

→ 5' V_k →
L L P A A Q P A M A D I E L T Q S P
T A T T A C C T G C T G C C A A C C A G C A T G G C G A C A T G A G T T C A C C A G T C T C

(SEQ ID NO. 264)

(SEQ ID NO. 265)

Fig.49.

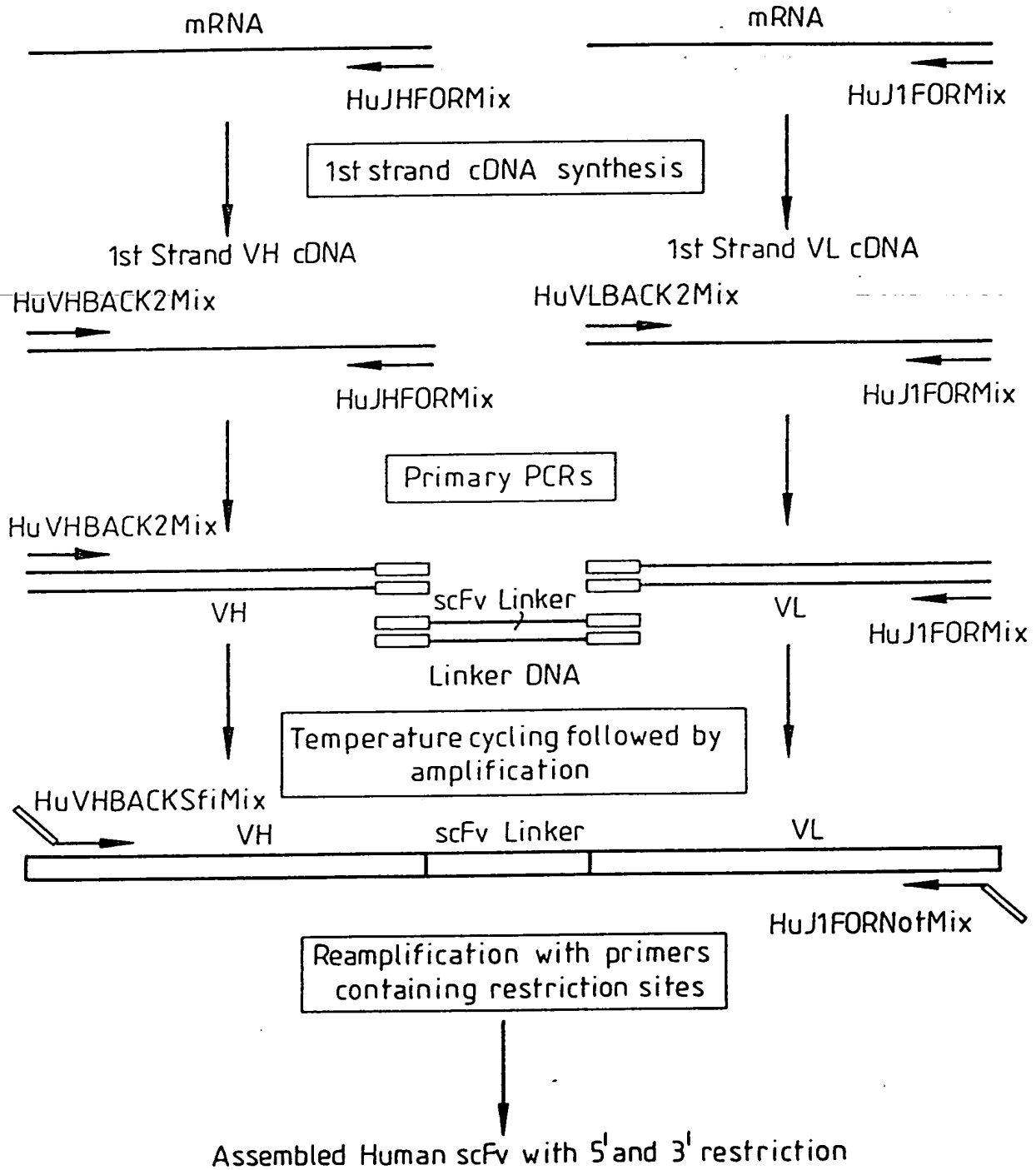


Fig.50a

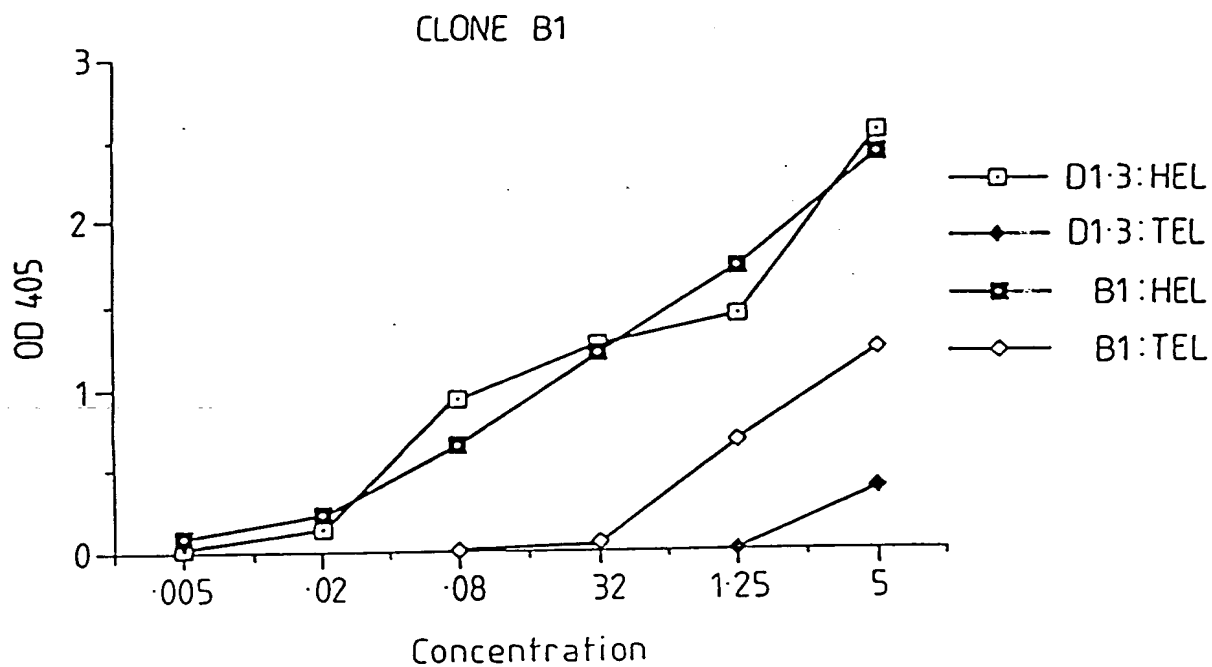


Fig.50b

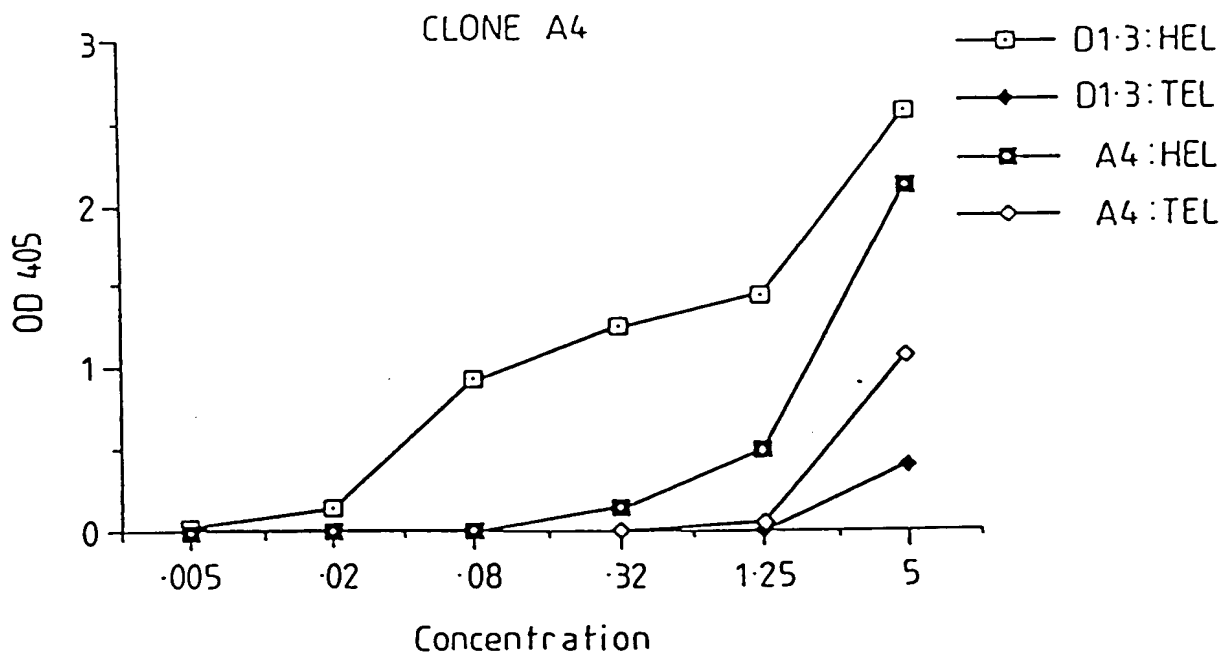


Fig.51.

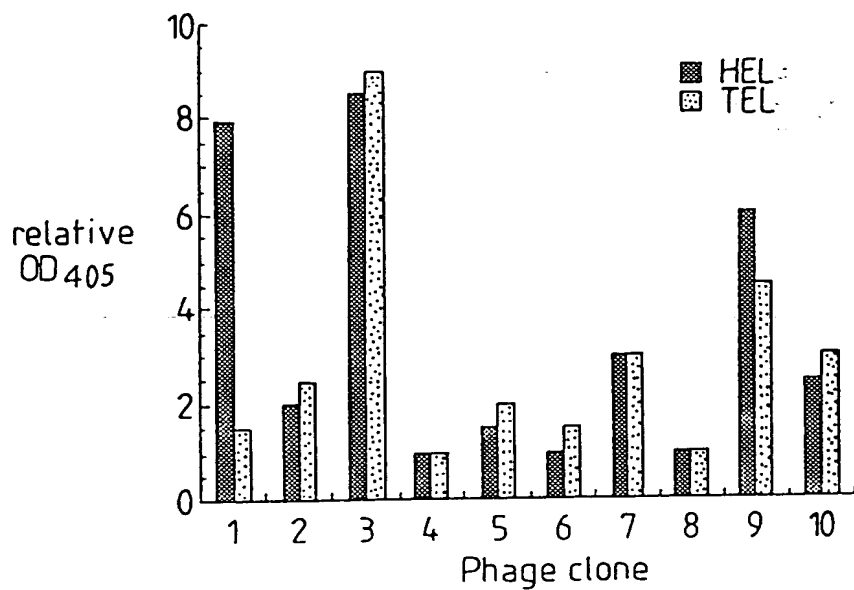


Fig.53.

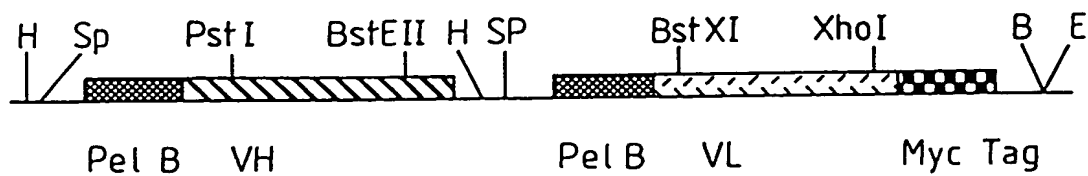




Fig.52.

CDR 1

CDR 2

D1.3 DIQMTQSPASLSASVGETVTITCRASGNIHNYLA WYQQKQKSPQLLVYYTTLAD
M1F DIELTQSPSSLSASLGERVSLTCRASQDIGSSLN WLQQEPDGTIKRLIYATSSLDS
M21 DIELTQSPALMAASPGEKVTITCSVSSSISSNLHWYQQKSETSPKPWIYGTSNLAS

CDR 3

D1.3 GVPSRFGSGGTQYSLKINSLQPEDFGSYQCQHFWSPTPTFGGGTKLEIKR
M1F GVPKRFGSRGSDYSLTISSESEDFVDYYCLQYASSPWTFGGGTKLELKR
M21 GVPVRFSGSGGTSYSLTISSEAEADAATYYCQQWSSYPLTFGAGTKLEIKR